

86482

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Michele Flood Examiner #: 77454 Date: 2/10/2003
 Art Unit: 1654 Phone Number 308-9432 Serial Number: 10/047,091
 Mail Box and Bldg/Room Location: 11D 13/11E11 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Hyaluronic acid gel, method of its production & medical material containing it

Inventors (please provide full names): Yoshiaki Miyata, Akio Okamoto, Masatoshi Kawata, Kazuhiro Oshima, Masamichi Hashimoto, and Kazuhiko Arai

Earliest Priority Filing Date: 8/2/1997

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Method of producing a hyaluronic acid gel comprising adjusting a hyaluronic acid solution to a pH 3.5 or below, and freezing and thawing the solution at least once, wherein the gel dissolves in a neutral aqueous solution at 37°C in 12 hours to a degree of dissolution of 50%; wherein the gel dissolves to yield solubilized hyaluronic acid having a molecular branched structure, partly containing a molecular weight fraction with a branching degree of at least 0.5 when treating under accelerating conditions for acid hydrolysis of hyaluronic acid.
 Gel not subjected to chemical crosslinking or chemical modification

Mary Jane Ruhi
 Tech. Info. Specialist, STIC
 TC-1600
 CM-1, Room 6A-06
 Phone: 605-1155

Claims Attached

STAFF USE ONLY

| STAFF USE ONLY | Type of Search | Vendors and cost where applicable |
|-----------------------------------------|-----------------------|-----------------------------------|
| Searcher: _____ | NA Sequence (#) _____ | STN 1 _____ |
| Searcher Phone # _____ | AA Sequence (#) _____ | Dialog _____ |
| Searcher Location: _____ | Structure (#) _____ | Questel/Orbit _____ |
| Date Searcher Picked Up: <u>2/14/03</u> | Bibliographic _____ | Dr. Link _____ |
| Date Completed: <u>2/21/03</u> | Litigation _____ | Lexis/Nexis _____ |
| Searcher Prep & Review Time: _____ | Fulltext _____ | Sequence Systems _____ |
| Clerical Prep Time: _____ | Patent Family _____ | WWW/Internet _____ |
| Online Time: _____ | Other _____ | Other (specify) _____ |

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L18 1 SEA FILE=REGISTRY ABB=ON "HYALURONIC ACID"/CN
 L19 12762 SEA FILE=HCAPLUS ABB=ON L18 OR ?HYALURONIC?(W)?ACID?
 L20 1653 SEA FILE=HCAPLUS ABB=ON L19 AND GEL?
 L21 857 SEA FILE=HCAPLUS ABB=ON L20 AND (?PRODN? OR ?PRODUCT? OR
 ?PREP? OR ?SYNTH?)
 L22 342 SEA FILE=HCAPLUS ABB=ON L21 AND (?METHOD? OR ?PROCED? OR
 ?PROCES? OR ?TECHNIQ? OR ?TECHNIC? OR ?MECHANISM?)
 L23 7 SEA FILE=HCAPLUS ABB=ON L22 AND (?MEDIC?(W)?MATER?)
 L24 25 SEA FILE=HCAPLUS ABB=ON L22 AND (?FREEZ? OR ?THAW?)
 L25 30 SEA FILE=HCAPLUS ABB=ON L23 OR L24
 L27 3 SEA FILE=HCAPLUS ABB=ON L22 AND PH(L) 3.5
 L28 32 SEA FILE=HCAPLUS ABB=ON L25 OR L27
 L29 2 SEA FILE=HCAPLUS ABB=ON L22 AND ?BRANCH?(W)?DEGREE?
 L30 32 SEA FILE=HCAPLUS ABB=ON L28 OR L29

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L30 ANSWER 1 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:76525 HCAPLUS

TITLE: Biodegradable injectable implants and related
methods of manufacture and use

INVENTOR(S): Caseres, Crisofo Peralta; D'Lagarde, Daniel Leon

PATENT ASSIGNEE(S): Medgraft Microtech, Inc., Mex.

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2003007782 | A2 | 20030130 | WO 2002-US20802 | 20020628 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: MX 2001-6732 A 20010629

US 2001-2283 A 20011205

AB This invention is directed to the field of medical implants, and more specifically to biodegradable injectable implants and their **methods** of manuf. and use. The injectable implants disclosed herein comprise glycolic acid and bio-compatible/bio-absorbable polymeric particles contg. a polymer of lactic acid. The particles are small enough to be injected through a needle but large enough to avoid engulfment by macrophages. The injectables of this invention may be in a pre-activated solid form or an activated form (e.g., injectable suspension or emulsion). For example, a lyophilized compn. was **prepd.** contg. glycolic acid 0.07 mg, poly(lactic acid) spheres 200.0 mg, hydroxypropyl Me cellulose 118.33 mg, D-mannitol 170.0 mg, pH stabilizer (phosphate buffer) 0.50 mg, and surfactant (Tween 80) 1.20 mg. The compn. was activated

extemporaneously with 5.5 mL water to obtain an injectable **prepn**

IT 9004-61-9, **Hyaluronic acid** 9004-61-9D
, **Hyaluronic acid**, esters
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**prepn.** of biodegradable injectable implants contg. glycolic
acid and particles of lactic acid polymers)

L30 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:60374 HCAPLUS

TITLE: The properties of chitosan-**gelatin** membranes
and scaffolds modified with **hyaluronic**
acid by different **methods**

AUTHOR(S): Mao, Jin Shu; Liu, Hai Feng; Yin, Yu Ji; Yao, Kang De

CORPORATE SOURCE: Research Institute of Polymeric Materials, Tianjin
University, Tianjin, 300072, Peop. Rep. China

SOURCE: Biomaterials (2003), 24(9), 1621-1629

CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The objective of the present study was to investigate the properties of
chitosan-**gelatin** membranes or scaffolds, which were modified by
incorporation of **hyaluronic acid** in the surface or
bulk phase through co-crosslinking with N,N-(3-dimethylamino-propyl)-N'-Et
carbodiimide (EDC) and N-hydroxysuccinimide (NHS) in 2-morpholinoethane
sulfonic acid (MES) buffer. The comparative study on properties of
surface modification (HA(S)) and polyblend membranes (HA(C)) revealed that
gelatin was enriched on the surface of HA(C), while
hyaluronic acid was enriched on the surface of the
HA(S). The HA(S) membranes made by surface modification **method**
had a characteristic surface morphol. The corresponding scaffolds were
prepd. through **freeze-drying**. The incorporation of
hyaluronic acid improved flexibility and fibroblasts
adhesion, while slowing down the rate of biodegrdn. of chitosan-
gelatin scaffold. Human fibroblasts adhered and proliferated well
on the membranes or scaffolds in vitro.

L30 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:978339 HCAPLUS

DOCUMENT NUMBER: 138:40111

TITLE: **Medical materials** sterilized by
radiation and their ways in use

INVENTOR(S): Gen, Shokyu

PATENT ASSIGNEE(S): Japan

SOURCE: U.S. Pat. Appl. Publ., 6 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2002197296 | A1 | 20021226 | US 2002-135122 | 20020430 |
| JP 2003000695 | A2 | 20030107 | JP 2001-228719 | 20010621 |
| EP 1270660 | A1 | 20030102 | EP 2002-13499 | 20020617 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: JP 2001-228719 A 20010621

AB The present invention provides **medical material** sterilized by radiation, comprising polymer composite using in living body, contg. multifunctional triazine compds. at wt. ratio range of 0.01 to 20% to the polymer. The present invention shows the fabrication of polymer composite having good heat and radiation resistance, by preventing heat molding record and irradiation on sterilized **processes** from deteriorating mol. wt. caused on heat and radiation decompn. of the polymer. It is possible that the polymer composite is applied for the medical field of decomposable and bio-absorbable polymers and even bio-nonabsorbent polymers such as suture of operation or bonding agent for broken bone as a result. Furthermore, it is possible that the polymer composite is applied for not only **medical material** but also food wrapping material of industrial use.

IT 9004-61-9, Hyaluronic acid

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**medical materials** sterilized by radiation and their ways in use)

L30 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:965151 HCAPLUS

DOCUMENT NUMBER: 138:35040

TITLE: Biocompatible, biodegradable, water-absorbent material prepared by polymer-polymer inter-coupling between a natural water-soluble polymer and a **synthetic** polymer

INVENTOR(S): Bucevschi, Mircea Dan; Colt, Monica

PATENT ASSIGNEE(S): Israel

SOURCE: U.S. Pat. Appl. Publ., 15 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| US 2002193516 | A1 | 20021219 | US 2001-823612 | 20010330 |
| PRIORITY APPLN. INFO.: | | | US 2001-823612 | 20010330 |

AB A bio-compatible, biodegradable macromol. water-absorbent polymeric material, which has a three-dimensional configuration with intermol. covalent bonds and contains free functional groups selected from OH, SH, NH₂, and COOH, is formed by polymer-polymer inter-coupling interaction between a natural water-sol. polymer A or its derivs. having a mol. wt. between 20,000 and 500,000 Da, and a **synthetic** polymer B at a ratio of A:B of 15:85-85:15 in a liq.-liq. heterogeneous system in the absence of any crosslinking or coupling agent. The natural polymer A, which can undergo polymer-polymer intercoupling reactions, can be selected from: a non-ionic natural, partially denatured or chem. modified polymer that does not dissociate in water; or an anionic natural, partially denatured or chem. modified polymer, that dissociates in water to form anions; or a cationic natural, partially denatured or chem. modified polymer, that dissociates in water to form cations; or an amphoteric natural, partially denatured or chem. modified polymer, that dissociates in water to form both anions and cations; or mixts. thereof. Thus, 20 g **gelatin** in 980 g of water is **prepd.** with 50 g NH₄OH (5%) added to give a pH of 8.5. A second 3862 g soln. contg. 80 g of poly(styrene-alt-maleic

anhydride), 700 cm³ of Et acetate, 3330 g OL1, and 300 cm³ N,N'-dimethylformamide, 292 g OL2, is added to the reaction vessel. In dropping funnel are introduced 250 g of 5% NH₄OH and an automated **titroprocessor** set to maintain the PH of the system at a const. value. The polymer-polymer intercoupling reaction in liq.-liq. heterogeneous system occurs in 150 min, and uses 180 g of 5% NH₄OH soln. Such superabsorbent materials that are biocompatible and biodegradable are useful in different applications, such as for bodily hygiene, **medical materials**, agromaterials, drying agents, and others.

IT **9004-61-9, Hyaluronic acid**

RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (biocompatible, biodegradable, water-absorbent material **prepd**
 . by polymer-polymer inter-coupling between a natural water-sol.
 polymer and a **synthetic** polymer)

L30 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:927270 HCAPLUS
 DOCUMENT NUMBER: 138:8352
 TITLE: Stable liquid formulations containing an antibody
 INVENTOR(S): Arvinte, Tudor; Fauquex, Pierre Francois
 PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen
 Verwaltungsgesellschaft M.B.H.; Genentech, Inc.
 SOURCE: PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2002096457 | A2 | 20021205 | WO 2002-EP6016 | 20020531 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |

PRIORITY APPLN. INFO.: GB 2001-13179 A 20010531

AB The present invention provides stable liq. formulations of antibodies suitable for parenteral administration. Also provided are aq. solns. which have high concns. of therapeutical antibodies which may be used to produce therapeutical liq. formulations. The present invention also relates to uses, such as medical uses, of the stable liq. formulations and **processes** for the **prodn.** of the stable liq. formulations. For example, a soln. of 40 mg/mL of RhuMAb E25 in the final **prodn.** buffer (contg. 0.02% Tween 20) was dialyzed against 0.1% acetic acid. The resulted E25 soln. in 0.1% acetic acid (still contg. Tween 20 detergent) was concd. by filtration through centrifugation to reach a concn. of 243 mg/mL E25. The soln. fluidity was similar to the fluidity of the solns. without Tween 20, showing that the detergent is compatible with the high protein concd. formulation.

IT **9004-61-9, Hyaluronic acid**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of stable aq. solns. of antibodies for allergy treatment)

L30 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:885564 HCAPLUS

TITLE: Dielectric study on various aqueous **gels** of polysaccharide

AUTHOR(S): Miura, Nobuhiro; Hashimoto, Tadashi; Goto, Masumi; Hayashi, Yoshihito; Shinyashiki, Naoki; Yagihara, Shin; Shigematsu, Teruyoshi; Shioya, Sumie; Nishida, Hirokazu; Dobashi, Toshiaki; Yoshii, Fumio

CORPORATE SOURCE: Department of Physics, Tokai University, Hiratsuka-shi, Kanagawa, 259-1292, Japan

SOURCE: Transactions of the Materials Research Society of Japan (2002), 27(3), 573-576
CODEN: TMRJE3; ISSN: 1382-3469

PUBLISHER: Materials Research Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We investigated dielec. property of aq. polysaccharide **gels** of CM-cellulose, **hyaluronic acid** and agarose by using a time domain reflectometry (TDR) and an impedance material analyzer over a frequency range of 1MHz-20GHz. We assigned a relaxation **process** due to free-water mols. around 10GHz and other relaxation **processes** at the lower frequency range. **Unfreezable** water was obsd. below a temp. **freezing** the free water T_f . Amt. of the water per a saccharide was calcd. and compared with that per an amide acid residue of globular protein and that per monomer unit of **synthetic** polymer.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:716325 HCAPLUS

DOCUMENT NUMBER: 137:246551

TITLE: Pharmaceutical compositions comprising crystals of polymeric carrier-stabilized antibodies and fragments for therapeutic uses

INVENTOR(S): Shenoy, Bhami; Govardhan, Chandrika P.; Yang, Mark X.; Margolin, Alexey L.

PATENT ASSIGNEE(S): Altus Biologics Inc., USA

SOURCE: PCT Int. Appl., 173 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2002072636 | A2 | 20020919 | WO 2001-US49628 | 20011226 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002136719 A1 20020926 US 2001-34950 20011226

PRIORITY APPLN. INFO.: US 2000-258704P P 20001228

AB **Methods** are also provided for **prepg.** stabilized formulations of whole antibody crystals or antibody fragment crystals using pharmaceutical ingredients or excipients and optionally encapsulating the crystals or crystal formulations in a polymeric carrier to produce compns. and using such protein crystals for biomedical applications, including delivery of therapeutic proteins and vaccines. Antibodies **prepd.** were Rituximab, Infliximab, Abciximab, Palivizumab, Murumonab-CD3, Gemtuzumab, Trastuzumab, Basiliximab, Daclizumab, Etanercept, and Ibiritumomab tiuxetan. These antibody **prepns.** are useful for treating cardiovascular disease, respiratory disease, transplant rejection, cancer, inflammatory disease, and for radioimmunotherapy.

IT **9004-61-9, Hyaluronic acid**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical compns. comprising crystals of polymeric carrier-stabilized antibodies and fragments for therapeutic uses)

L30 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:185694 HCAPLUS

DOCUMENT NUMBER: 136:252483

TITLE: Clear oil-containing pharmaceutical compositions containing a therapeutic agent

INVENTOR(S): Chen, Feng-Jing; Patel, Mahesh V.; Fikstad, David T.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 45 pp., Cont.-in-part of U.S. Ser. No. 751,968.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2002032171 | A1 | 20020314 | US 2001-877541 | 20010608 |
| US 6267985 | B1 | 20010731 | US 1999-345615 | 19990630 |
| US 6309663 | B1 | 20011030 | US 1999-375636 | 19990817 |
| US 2001024658 | A1 | 20010927 | US 2000-751968 | 20001229 |
| US 6458383 | B2 | 20021001 | | |

PRIORITY APPLN. INFO.: US 1999-345615 A2 19990630
US 1999-375636 A2 19990817
US 2000-751968 A2 20001229
WO 2000-US18807 A 20000710

AB The present invention relates to pharmaceutical compns. and **methods** for improved solubilization of triglycerides and improved delivery of therapeutic agents. Compns. of the present invention include a carrier, where the carrier is formed from a combination of a triglyceride and at least 2 surfactants, at least one of which is hydrophilic. Upon diln. with an aq. medium, the carrier forms a clear, aq. dispersion of the triglyceride and surfactants. Thus, a formulation contained soybean oil, 80, Tween-20 200, and Tween-80 800 mg.

IT **9004-61-9, Hyaluronic acid**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clear oil-contg. pharmaceutical compns. contg. therapeutic agent)

L30 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:107189 HCAPLUS

DOCUMENT NUMBER: 136:172828

TITLE: Bioabsorbable composites of derivatized
hyaluronic acid

INVENTOR(S): Sadozai, Khalid K.; Kuo, Jing-Wen; Sherwood, Charles
H.

PATENT ASSIGNEE(S): Anika Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2002009792 | A1 | 20020207 | WO 2001-US40794 | 20010522 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |

US 2002071855 A1 20020613 US 2001-863029 20010522

PRIORITY APPLN. INFO.: US 2000-222116P P 20000728

OTHER SOURCE(S): MARPAT 136:172828

AB The present invention relates to a composite and a **method** for reducing post-operative adhesion of tissues. The composite includes a biocompatible, biodegradable support, and a water-insol. **hyaluronic acid** deriv. at the support. The **hyaluronic acid** deriv. includes an N-acylurea that results from crosslinking by the reaction of **hyaluronic acid** with a multifunctional carbodiimide. Optionally, a monocarbodiimide also may be employed. A pharmaceutically-active mol. may be added to the N-acylurea deriv. of **hyaluronic acid**. Although the composite includes material that prevents adhesion between tissues, in order to reduce the need for suturing when the composite is being used during a surgical **procedure**, a material that enhances adhesion of the composite to tissues may be applied to a surface of the composite. A **method** of forming the composite for reducing post-operative adhesion of tissues, including the step of applying an N-acylurea deriv. of **hyaluronic acid** resulting from crosslinking with a multifunctional carbodiimide, to a biocompatible, biodegradable support; a **method** of **prepg.** a drug delivery vehicle that includes a pharmaceutically-active mol. with the N-acylurea deriv. of **hyaluronic acid** resulting from crosslinking with a multifunctional carbodiimide; and a **method** of reducing post-operative adhesion of tissues are disclosed. A biscarbodiimide, p-phenylenebis(ethylcarbodiimide), and HA were reacted at a molar equiv ratio of 16.7% to yield a water-insol. **gel**. This **gel** was poured into an 8 cm x 8 cm mold under aseptic conditions.

The mold contg. the crosslinked HA **gel** was frozen at -45.degree. and then **freeze**-dried for 24 h under vacuum of <10 mm. The **freeze**-dried sponge was compressed under aseptic conditions and cut into 4 cm x 4 cm pieces. These sponges were put in sterile pouches and sealed to keep them sterile.

IT **9004-61-9D, Hyaluronic acid**, derivs.

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioabsorbable composites of derivatized **hyaluronic acid**)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:868278 HCAPLUS

DOCUMENT NUMBER: 136:11093

TITLE: Transfection system to promote wound healing

INVENTOR(S): Andree, Christoph; Voigt, Matthias; Stark, G. Bjoern

PATENT ASSIGNEE(S): Klinikum der Albert-Ludwigs-Universitaet Freiburg, Germany

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|------------------|----------|
| WO 2001089593 | A1 | 20011129 | WO 2001-EP5937 | 20010523 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| DE 10025609 | A1 | 20011213 | DE 2000-10025609 | 20000524 |

PRIORITY APPLN. INFO.: DE 2000-10025609 A 20000524

AB The present invention relates to a **method** of **prepg.** a compn. for wound healing, and for repairing and regenerating human and animal tissue, said **method** comprising the following steps: a) providing a plasmid DNA in substantially pure form, which encodes a gene that has a pos. effect on the progression of the regeneration of the tissue, b) providing a component/components of a self-hardening bio-polymer, and c) providing a cell suspension with cells which promote regeneration, characterized in that components (a), (b) and (c) are incubated with each other simultaneously or successively so that the plasmid and the cell suspension are obtained homogeneously distributed in one of the biopolymer components.

IT **9004-61-9, Hyaluronic acid**

RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(transfection system to promote wound healing)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:780648 HCAPLUS
 DOCUMENT NUMBER: 135:335147
 TITLE: Polymer-based injectable sustained release
 pharmaceutical compositions for peptide and protein
 drugs
 INVENTOR(S): Lee, Hee-yong; Lee, Hye-suk; Kim, Jung-soo; Kim,
 Sang-beom; Lee, Ji-suk; Choi, Ho-il; Chang, Seung-gu
 PATENT ASSIGNEE(S): Pepton Inc., S. Korea
 SOURCE: PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 2001078687 | A1 | 20011025 | WO 2001-KR462 | 20010322 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1187602 | A1 | 20020320 | EP 2001-917893 | 20010322 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 2003026844 | A1 | 20030206 | US 2002-18870 | 20020418 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | KR 2000-20484 | A 20000418 |
| | | | KR 2000-49344 | A 20000824 |
| | | | WO 2001-KR462 | W 20010322 |

AB Controlled and sustained release injectable pharmaceutical compns. for a biopharmaceutical, such as peptides and proteins are described. **Processes for prepn.** of an injectable sustained release compn. comprises (i) a step of **prepg.** biodegradable porous microspheres having accessible ionic functional groups, (ii) a step of encapsulating a biopharmaceutical into the microspheres through ionic interaction by suspending or equilibrating the microspheres in a soln. contg. the biopharmaceutical, and (iii) a step of recovering and **freeze**-drying the biopharmaceutical-incorporated microspheres. For example, microspheres were **prepd.** by water/oil/water double emulsion solvent evapn. **method** using a hydrophilic 50:50 PLGA polymer (RG 502H), which contains free carboxy end groups. Deionized water (800 mL) was added to 1 g of PLGA polymer dissolved in 2 mL of methylene chloride and emulsified by sonication for 30 s using a probe type ultrasonic generator. This primary emulsion was dispersed into 200 mL of deionized water contg. 0.5% polyvinyl alc. (wt./vol.) in a vessel which connected to a const. temp. controller and mixed well by stirring for 15 min at 2500 rpm, 25.degree. using a mixer. After mixing for another 15 min at 1500 rpm, 25.degree., temp. of continuous phase was increased to 40.degree. to evap. methylene chloride. After 1 h stirring at 40.degree., 1500 rpm, temp. was decreased to 25.degree.. The hardened microspheres were collected by centrifugation and washed twice with 200 mL

of deionized water, and then **freeze**-dried. The microspheres obtained were used for incorporation of protein drugs, i.e., ovalbumin, bovine serum albumin, human growth hormone, RNase A, or lysozyme through ionic interaction by simply soaking and equilibrating the microspheres into a buffer soln. having an appropriate concn. of protein.

IT 9004-61-9, **Hyaluronic acid**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**prepn.** of polymer-based injectable sustained-release microspheres for peptide and protein drugs)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:713195 HCAPLUS

DOCUMENT NUMBER: 135:262308

TITLE: Polymeric composite materials and their manufacture

INVENTOR(S): Coombes, Allan Gerald Arthur; Downes, Sandra; Griffin, Martin

PATENT ASSIGNEE(S): University of Nottingham, UK; Nottingham Trent University

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2001070293 | A1 | 20010927 | WO 2001-GB1177 | 20010319 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: GB 2000-6439 A 20000318

AB A **method** for the **prepn.** of a polymeric composite material comprises the steps of (a) forming a porous body of a first polymer; (b) impregnating said porous body with a soln. of a second polymer; and (c) causing or allowing solvent to evap. from said body. The first polymer is preferably a natural polymer, e.g. collagen, and the second polymer is preferably a **synthetic** polymer, e.g. a polymer selected from the group consisting of poly(.alpha.-hydroxy acid) such as polylactide, poly(DL-lactide-co-glycolide), poly(.epsilon.-caprolactone), polyorthoesters, polyphosphazenes, **hyaluronic acid** esters, polyanhydrides, copolymers of such polymers and blends thereof. The composites are particularly useful in medical and biomedical applications. For example, collagen/polycaprolactone biocomposites were produced by **freeze** drying 2 mL of 0.25% collagen soln. and impregnation of lyophilized collagen within 2 mL of a polycaprolactone soln. in dichloromethane, followed by solvent evapn. The biocomposite revealed a highly porous morphol. and virtually complete coverage of the collagen component by polycaprolactone. A major fraction (approx. 70-100%) of the collagen content of biocomposites is accessible for

digestion by collagenase indicating a high degree of collagen exposure/presentation for interaction with other extracellular matrix proteins or cells contacting the biomaterial surface.

IT 9004-61-9, Hyaluronic acid 9004-61-9D

, Hyaluronic acid, esters

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(manuf. of polymeric composite materials for biomedical uses)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:584542 HCAPLUS

DOCUMENT NUMBER: 136:236773

TITLE: Hyaluronan molecular weight and polydispersity in some commercial intra-articular injectable **preparations** and in synovial fluid

AUTHOR(S): Adam, N.; Ghosh, P.

CORPORATE SOURCE: Institute of Bone and Joint Research, Department of Surgery, Royal North Shore Hospital, University of Sydney, St. Leonards, 2065, Australia

SOURCE: Inflammation Research (2001), 50(6), 294-299
CODEN: INREFB; ISSN: 1023-3830

PUBLISHER: Birkhaeuser Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Objective and Design: Hyaluronan is the major non-proteinaceous component of joint synovial fluid and is responsible for the unique rheol. and biol. properties of this medium. In joint arthropathies the mol. wt. and concn. of hyaluronan may change, thereby influencing joint physiol. and function. Intra-articular administered hyaluronan derived from a no. of sources, has been used for the treatment of osteoarthritis, however, there is limited information on the mol. wt. and polydispersity of these various com. **prepn.** The objective of this study was to develop an accurate, convenient **method** by which the mol. wt. and polydispersity of hyaluronan may be detd. and then applied to characterize the hyaluronan in synovial fluid. **Materials and Methods:** Characterization of the mol. parameters of hyaluronan of different sources and in ovine synovial fluid was accomplished by a multi-angle laser-light scattering (MALLS) detector coupled to a **gel** permeation chromatog. (GPC) system, fitted with an automatic sample injector. Conclusion: Seven com. available hyaluronan **prepn.** of reported mol. wt. were analyzed. The wt. av. mol. wt. (Mw) and no. av. mol. wt. (Mn) values obtained for 6 of the 7 **prepn.** using the MALLS-GPC system were in good agreement with the reported values. The abnormally low values for the exception suggested that degrdn. of hyaluronan had occurred. The MALLS-GPC **technique** was then used to det. the mol. characteristics of the endogenous hyaluronan in normal ovine synovial fluids. While the Mws ranged from <1 .times. 106 to 7 .times. 106 Da, the majority were between 1 .times. 106-3 .times. 106 Da. The effects of **freezing** and **thawing** synovial fluid upon mol. wt. of hyaluronan were also investigated and were found to diminish both Mz and Mw values.

IT 9004-61-9, Hyaluronan

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hyaluronan mol. wt. and polydispersity in intra-articular injectable **prepn.** and in synovial fluid)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:581969 HCAPLUS

DOCUMENT NUMBER: 135:138985

TITLE: Controlling of pore structure of water-soluble
polymeric spongy molding as **medical
material**

INVENTOR(S): Sugie, Toshimasa; Yanagawa, Hiroaki; Baba, Yuji

PATENT ASSIGNEE(S): Menicon Co., Ltd., Japan

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 2001057121 | A1 | 20010809 | WO 2001-JP698 | 20010201 |
| W: CN, IN, JP, KR, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| EP 1273615 | A1 | 20030108 | EP 2001-948993 | 20010201 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| US 2003015825 | A1 | 20030123 | US 2002-181949 | 20020801 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | JP 2000-26774 | A 20000203 |
| | | | WO 2001-JP698 | W 20010201 |

AB Title **process**, by which phys. connection between the inside and the outside of a polymeric spongy molding is facilitated through pore structure, comprises (A) a **pre-freezing** step in which a soln./**gel** of a water-sol. polymeric material is cooled on its side contacting air, so as to result in a temp. gradient, parallel to the thickness direction, inside the soln./**gel**; and (B) a step in which the preliminarily frozen soln./**gel** is **freeze** -dried.

IT **9004-61-9, Hyaluronic acid**

RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(prepn. porous water-sol. polymeric spongy molding as **medical material**)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:78175 HCAPLUS

DOCUMENT NUMBER: 134:136705

TITLE: **Hyaluronic acid** anti-adhesion
barrier

INVENTOR(S): Zhang, Gary

PATENT ASSIGNEE(S): United States Surgical Corporation, USA

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 2001006973 | A1 | 20010201 | WO 2000-US40491 | 20000726 |
| W: AU, CA, JP, MX, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 1207828 | A1 | 20020529 | EP 2000-965568 | 20000726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| US 2002141968 | A1 | 20021003 | US 2001-36239 | 20011228 |
| PRIORITY APPLN. INFO.: | | | US 1999-146065P | P 19990728 |
| | | | WO 2000-US40491 | W 20000726 |

AB **Methods** of forming crosslinked **hyaluronic acid** anti-adhesion barriers, crosslinked **hyaluronic acid** anti-adhesions barriers, **methods** for preventing or inhibiting adhesions, and **methods** of promoting healing of a wound are provided. The **method** of forming the crosslinked **hyaluronic acid** anti-adhesion barrier includes **freeze-drying** a soln. including **hyaluronic acid** to form a **hyaluronic acid** foam, which is then reacted with a crosslinking agent to form a crosslinked **hyaluronic acid** foam. The crosslinked **hyaluronic acid** foam is mixed with a soln. contg. **hyaluronic acid** to form an anti-adhesion barrier. An anti-adhesion barrier **gel** **prepd.** according to above **method** was used to prevent adhesion formation between the cecum and the peritoneal wall in the rats. Incidence of adhesion formation at 7 days following the use of **hyaluronic acid gel** was significantly decreased.

IT **9004-61-9, Hyaluronic acid**

RL: RCT (Reactant); RACT (Reactant or reagent)
(**hyaluronic acid** anti-adhesion barrier)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:592778 HCAPLUS

DOCUMENT NUMBER: 133:179212

TITLE: **Hyaluronic acid gel**
compositions without crosslinking agents and modifiers
useful as **medical materials** and
their **preparation methods**

INVENTOR(S): Hashimoto, Masamichi; Umeda, Toshihiko; Arai, Kazuhiko; Miyata, Yoshiaki; Yamamoto, Osamu; Himeda, Yasukazu

PATENT ASSIGNEE(S): Denki Kagaku Kogyo Kabushiki Kaisha, Japan

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2000049084 | A1 | 20000824 | WO 2000-JP946 | 20000218 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1174463 A1 20020123 EP 2000-904045 20000218

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: JP 1999-42371 A 19990219
JP 1999-318579 A 19991109
WO 2000-JP946 W 20000218

AB The compns. with good biocompatibility and slow release, useful for adhesion prevention and wound dressing, are obtained by mixing a **hyaluronic acid** with a polymeric compd. in an aq. soln. at a pH <3.5, then **freezing** and **thawing** where the polymeric compd. is chosen from CM-cellulose, polysaccharides, proteins, nucleic acids or **synthetic** polymers.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT.

L30 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:585450 HCAPLUS

DOCUMENT NUMBER: 133:183073

TITLE: Bone repair materials containing **gel** comprising from only **hyaluronic acid**

INVENTOR(S): Hashimoto, Masamichi; Arai, Kazuhiko

PATENT ASSIGNEE(S): Denki Kagaku Kogyo K. K., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| JP 2000230002 | A2 | 20000822 | JP 1999-31527 | 19990209 |
| PRIORITY APPLN. INFO.: | | | JP 1999-31527 | 19990209 |

AB The materials, used for repair bone defects due to injury and tooth extn., etc., comprise **gel prepd.** from only **hyaluronic acid** (I) which is poorly-sol. in neutral aq. solns. The **gel** may be in the forms of films, sheets, slurry, crushed **products**, sponge, lump, or paste. The materials may comprise (A) I **gel**, which shows dissoln. rate in a neutral aq. soln. at 37.degree. after 12 h .ltoreq.50%, have branched structure when solubilized upon accelerated acid hydrolysis, and partly contains a fraction with **branching degree** .gtoreq.0.5 in the hydrolyzates, (B) .gtoreq.1 selected from ungelatinized I, bioactive substances, bone granules, and antibiotics. Na hyaluronate was dissolved in H2O at 1% and the soln. was adjusted to pH 1.5 with HCl. The acidic soln. was frozen in a glass bottle at -20.degree. for 22 h and **thawed** at 25.degree. for 2 h. The **freezing-thawing process** was repeated twice, and the **product** was soaked in phosphate-buffered saline at 5.degree. for

24 h, and then **freeze**-dried to give sponge **gel**.
Application of the sponge **gel** to pit formed on a skull of rabbits regenerated bone.

IT **9004-61-9, Hyaluronic acid**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone repair materials contg. **gel** comprising from only **hyaluronic acid**)

L30 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:335252 HCAPLUS

DOCUMENT NUMBER: 132:326100

TITLE: **Hyaluronic acid gel, process** for the **preparation** thereof and **medical materials** containing the same

INVENTOR(S): Miyoshi, Teruzou; Kitagawa, Hironoshin; Arai, Kazuhiko; Kaneko, Hiroshi; Umeda, Toshihiko

PATENT ASSIGNEE(S): Denki Kagaku Kogyo Kabushiki Kaisha, Japan

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2000027405 | A1 | 20000518 | WO 1999-JP6232 | 19991109 |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2000010797 | A5 | 20000529 | AU 2000-10797 | 19991109 |
| EP 1129683 | A1 | 20010905 | EP 1999-954451 | 19991109 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |

PRIORITY APPLN. INFO.: JP 1998-318969 A 19981110
JP 1999-5424 A 19990112
JP 1999-18017 A 19990127
JP 1999-33974 A 19990212
JP 1999-42372 A 19990219
WO 1999-JP6232 W 19991109

AB The invention relates to a **hyaluronic acid gel** made of **hyaluronic acid** alone, which is difficultly sol. in aq. neutral solns. and has such a fluidity as to permit easy ejection from syringes. An injection contg. **hyaluronic acid gel** is useful in treating e.g. arthritis.

IT **9004-61-9, Hyaluronic acid**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hyaluronic acid gel, process** for the **prepn.** thereof and **medical materials** contg. the same)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2000:302121 HCAPLUS
 DOCUMENT NUMBER: 132:326090
 TITLE: Wound-healing agents comprising **gel** formed
 only from **hyaluronic acid**
 INVENTOR(S): Arai, Kazuhiko
 PATENT ASSIGNEE(S): Denki Kagaku Kogyo K. K., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| JP 2000128789 | A2 | 20000509 | JP 1998-307104 | 19981028 |
| PRIORITY APPLN. INFO.: | | | JP 1998-307104 | 19981028 |

AB The wound healing agents, useful for treatment of burn, ulcer, decubitus, tympanic membrane perforation, etc., comprise **gel** formed from only **hyaluronic acid** (I) which is poorly-sol. in neutral aq. solns. I should be satisfy the following physicochem. properties: (1) dissoln. rate in a neutral aq. soln. at 37.degree. after 12 h is .ltoreq.50% and (2) I solubilized by accelerated hydrolysis of I has branched structure and partly contains a fraction with **branching degree** .gtoreq.0.5. The **gel** may be in the forms of sheets, films, crushed **products**, sponges, lumps, fibers, or tubes. The wound healing agents may contain ungelled I in addn. to the **gel**. Na hyaluronate (mol. wt. 2 .times. 106 Da) was dissolved in H2O to 1 wt.%, and the soln. was adjusted to pH 1.5 with HCl. The acidic soln. was frozen at -20.degree. for 22 h and **thawed** at 25.degree. for 2 h. The **process** was repeated twice to give a spongy **product**, which was soaked in a phosphate-buffered saline (pH 7) at 5.degree. for 24 h, washed with H2O, and then **freeze**-dried to give a poorly water-sol. sheet of I **gel**. Wound healing-promoting effect of the sheet on full-thickness dermal wound by excision in rats was examd.

IT **9004-61-9, Hyaluronic acid**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (wound-healing agents in forms of sheets, sponges, fibers, tubes, and comprising **gel** formed only from **hyaluronic acid** which is poorly-sol. in neutral aq. solns.)

L30 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1999:48647 HCAPLUS
 DOCUMENT NUMBER: 130:129972
 TITLE: Pharmaceutical **gels** containing hydrophilic polymer
 INVENTOR(S): Schoenfeldt, Lars; Nielsen, Brian; Ayzma, Josef
 PATENT ASSIGNEE(S): Coloplast A/S, Den.
 SOURCE: PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 9901166 | A1 | 19990114 | WO 1998-DK298 | 19980702 |
| W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9879087 | A1 | 19990125 | AU 1998-79087 | 19980702 |
| EP 994733 | A1 | 20000426 | EP 1998-929248 | 19980702 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| US 2002172708 | A1 | 20021121 | US 2000-446902 | 20000317 |
| PRIORITY APPLN. INFO.: | | | DK 1997-789 | A 19970702 |
| | | | WO 1998-DK298 | W 19980702 |

AB Pharmaceutical **gels** contain a non-fibrous porous material essentially consisting of one or more hydrophilic polymeric component(s) or one or more hydrophilic polymeric component(s) and one or more pharmaceutical medicaments, said **method** comprising forming an aq. soln., sol or **gel** comprising one or more hydrophilic polymers and/or pharmaceutical medicaments, **freezing** or foaming the soln., dehydrating the frozen or foamed soln. leaving a non-fibrous porous material in a solid, porous form, and optionally subjecting the resulting porous material to a dry heat treatment. A crosslinked xerogel having controlled morphol. was **prepd.** by mixing 40.0 g of a 2.00% sodium alginate soln. with 40.0 g of a 2.00% crosslinked CM-cellulose soln., and stirred. To the above mixt. was added 14.0 g of a 2.00% calcium alginate soln. and 3.00 g of a 13.2.00% calcium chloride dihydrate soln. and mixed to obtain a homogeneous sol **gel**. The sol **gel** was frozen into sheets with a thickness of 4 mm and **freeze**-dried.

IT 9004-61-9, Hyaluronic acid

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical **gels** contg. hydrophilic polymeric)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:351803 HCAPLUS

DOCUMENT NUMBER: 128:326576

TITLE: Collagen material and **process** for producing it

INVENTOR(S): Shimizu, Yasuhiko

PATENT ASSIGNEE(S): Topic International Co., Ltd., Japan; Shimizu, Yasuhiko

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9822157 | A1 | 19980528 | WO 1997-JP4205 | 19971119 |
| W: CA, CN, JP, KR, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 943346 | A1 | 19990922 | EP 1997-912506 | 19971119 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, MC, IE, FI | | | | |
| CN 1237913 | A | 19991208 | CN 1997-199925 | 19971119 |
| KR 2000057131 | A | 20000915 | KR 1999-704398 | 19990519 |
| US 6277397 | B1 | 20010821 | US 1999-308557 | 19990520 |
| US 2001016205 | A1 | 20010823 | US 2001-761593 | 20010116 |
| US 6440167 | B2 | 20020827 | | |

PRIORITY APPLN. INFO.:

| | | |
|----------------|----|----------|
| JP 1996-308856 | A | 19961120 |
| JP 1996-308857 | A | 19961120 |
| JP 1997-263374 | A | 19970929 |
| WO 1997-JP4205 | W | 19971119 |
| US 1999-308557 | A3 | 19990520 |

AB The invention relates to a collagen material comprising a laminate of a multilayer structure of an ultrafine fibrous nonwoven fabric of collagen sandwiched between nonfibrillated collagen layers; a filamentous material comprising the collagen material; a **process** for producing the same; and a **medical material** comprising the collagen material, particularly a medical film substitute comprising the **medical material**. These materials are produced from collagen without using **synthetic** polymer material, have such a property as to permit suturing while maintaining the biochem. characteristics inherent in collagen. Further, the medical film substitute can be used as a material for making up for a defective portion of a biol. membrane, such as a dura mater, heart sac, pleura, peritoneum, or chorion, poses no moral problem, can be stably supplied, have no fear of infection, causes no denaturation of cells, can control the degrading rate after application to the organism, and can promote the regeneration of a biol. membrane.

IT 9004-61-9, Hyaluronic acid

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(collagen material for medical use and **process** for producing it)

L30 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:443310 HCAPLUS

DOCUMENT NUMBER: 127:52465

TITLE: Photocured crosslinked **hyaluronic acid gel** and **method of preparation** thereof

INVENTOR(S): Waki, Michinori; Miyamoto, Kenji

PATENT ASSIGNEE(S): Seikagaku Corporation, Japan; Waki, Michinori; Miyamoto, Kenji

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

WO 9718244 A1 19970522 WO 1996-JP3349 19961114
 W: AU, CA, CN, HU, JP, KR, NO, RU, US
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 CA 2237192 AA 19970522 CA 1996-2237192 19961114
 AU 9675872 A1 19970605 AU 1996-75872 19961114
 AU 722250 B2 20000727
 EP 861270 A1 19980902 EP 1996-938473 19961114
 EP 861270 B1 20020724
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, FI
 CN 1207744 A 19990210 CN 1996-199650 19961114
 CN 1098863 B 20030115
 JP 11512778 T2 19991102 JP 1996-518745 19961114
 AT 221086 E 20020815 AT 1996-938473 19961114
 ES 2179215 T3 20030116 ES 1996-938473 19961114
 US 6031017 A 20000229 US 1998-68227 19980505
 NO 9802212 A 19980714 NO 1998-2212 19980514
 PRIORITY APPLN. INFO.: JP 1995-319825 A 19951115
 WO 1996-JP3349 W 19961114

AB A photocured crosslinked **hyaluronic acid gel**, which has a storage modulus (G') of 50-1500 Pa, a loss modulus (G'') of 10-300 Pa, and a tangent delta (G''/G') of 0.1-0.8 in dynamic viscoelasticity at a frequency of 10 Hz, and which is a hydrogel obtained by irradiation with UV rays of a photoreactive **hyaluronic acid** deriv. in which a photoreactive crosslinking group is chem. linked to a functional group of the **hyaluronic acid** and crosslinking of mutual photoreactive crosslinking groups, **methods** for **prepg.** the same, and uses thereof as **biomedical materials** are disclosed. A such **hyaluronic acid** (I) deriv. was **prepd.** from I and 6-aminohexyl cinnamate HCl-salt.

L30 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:145273 HCAPLUS
 DOCUMENT NUMBER: 126:141392
 TITLE: Cellulases with reduced mobility by immobilization or **gel** incorporation for use in laundry detergents or fabric softeners
 INVENTOR(S): Nielsen, Jack Bech; Tikhomirov, Dmitry Feodorovich
 PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.; Nielsen, Jack Bech; Tikhomirov, Dmitry Feodorovich
 SOURCE: PCT Int. Appl., 77 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9701629 | A1 | 19970116 | WO 1996-DK284 | 19960626 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA | | | | |
| AU 9662988 | A1 | 19970130 | AU 1996-62988 | 19960626 |
| EP 835302 | A1 | 19980415 | EP 1996-921912 | 19960626 |

R: BE, DE, DK, ES, FR, GB, GR, IT, NL, SE, PT, IE

PRIORITY APPLN. INFO.:

DK 1995-750

19950628

WO 1996-DK284

19960626

AB A cellulolytic enzyme **prepn.** comprising a cellulase with reduced mobility is **prepd.**, e.g., by increasing the mol. wt. or apparent size of the cellulase protein mol. or by insolubilizing or immobilizing the cellulase. The cellulase component may be immobilized by incorporation into a **gel**, by the formation of stable or temporary aggregates with enhanced mol. mass, by rapid immobilization of cellulase protein on insol. components, by rapid autoimmobilization of the cellulase protein, or by adsorption to an insol. or sol. carrier. The carrier is preferably a cellulose-contg. carrier of fibrous, microcryst., or amorphous structure, and more preferably a sol. or insol. polymer, esp. a polysaccharide capable of interaction with the enzyme via a cellulose binding domain (CBD) or catalytic domain, or a sol. polycationic cellulose deriv. For example, Humicola insolens 43-kDa cellulase (1.6 g/L) may be autoimmobilized on 100 g/L Avicel (microcryst. cellulose) by incubation in sodium phosphate buffer (0.05M, pH 7.5) at 20.degree. for 30 min, repeated centrifugation at 4000 rpm for 15 min and 5.degree., **freezing** the moist sediment, and milling. About 50% of the total cellulase is autoimmobilized by this **procedure**, and the immobilized cellulase retains full activity as "free" cellulase. The cellulase **prepn.** has a much lesser effect or influence on the durability or aging behavior of the cellulosic substrate than corresponding unmodified cellulases while at least having as good an effect on the look or feel, when used for treatment of cellulosic fabrics or textiles. The cellulase **prepn.** may be used for domestic or industrial laundering or fabric softening as an ingredient of a detergent compn., for bio-polishing, or for stone-washing denim fabric or denim jeans or other dyed fabric or garments.

IT 9004-61-9, Hyaluronic acid

RL: NUU (Other use, unclassified); USES (Uses)

(cellulases with reduced mobility by immobilization or **gel**

incorporation for use in laundry detergents or fabric softeners)

L30 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:728977 HCAPLUS

DOCUMENT NUMBER: 126:3770

TITLE: BH55 hyaluronidase

INVENTOR(S): Stern, Robert; Frost, Gregory I.; Hall, Jackson; Shuster, Svetlana; Formby, Bent; Colbern, Gail T.

PATENT ASSIGNEE(S): Regents of the University of California, USA; Sansum Medical Research Foundation; California Pacific Medical Center, Research Institute

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9631596 | A1 | 19961010 | WO 1996-US4448 | 19960328 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5747027 | A | 19980505 | US 1995-419594 | 19950407 |
| US 5827721 | A | 19981027 | US 1997-919089 | 19970827 |

PRIORITY APPLN. INFO.:

US 1995-419594

19950407

AB A purified hyaluronidase BH55 polypeptide isolated from a mammalian species, preferably bovine or human, is provided. The invention also features DNA encoding BH55, vectors and transformed host cells contg. DNA encoding BH55, **methods** of making BH55 hyaluronidase polypeptides, and antibodies that specifically bind BH55. Thus, a second new hyaluronidase termed BH55 is found in com. available bovine testicular exts. which is distinct from the known PH20 isoform. BH55 is purified from a com. **prepn.** (2.8% yield, 8-fold) through sequential affinity chromatog. on Con A-Sepharose, cation exchange on MONO-S (FPLC), and **gel** filtration on Superose 12 (FPLC). BH55 hyaluronidase has the following characteristics: (1) .beta.-1,4-endoglycosidase activity in the cleavage of **hyaluronic acid**; (2) a mol. wt. ranging from about 14 kDa to 55 kDa, and a mol. wt. of about 55 kDa on SDS-PAGE; (3) immunol. cross-reactivity with an anti-porcine liver hyaluronidase antibody; (4) a specific enzymic activity of .apprx.70 .times. 103 turbidity reducing units (TRU)/mg protein following purifn., (5) is stabilized in 1 mg/mL polyvinyl alc., sodium chloride; (6) is inhibited in the presence of heparin or melittin; (7) is destabilized at **pH** below 4.0 and loses >70% of its activity after 1 h incubation at **pH 3.5** at 37.degree.; and (8) contains specific amino acid sequences. The design of oligonucleotide probes based upon detd. N-terminal and CNBr amino acid sequences, and the cloning of DNA encoding bovine and human BH55, are also described.

L30 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:452652 HCAPLUS

DOCUMENT NUMBER: 125:123812

TITLE: Composition for repair of defects in osseous tissues, **method** of making, and prosthesis

INVENTOR(S): Wolfenbarger, Lloyd, Jr.

PATENT ASSIGNEE(S): Bioscience Consultants, USA

SOURCE: U.S., 8 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| US 5531791 | A | 19960702 | US 1993-95020 | 19930723 |
| PRIORITY APPLN. INFO.: | | | US 1993-95020 | 19930723 |

AB A biocompatible collagen/demineralized human bone composite material, **method** for making the same, and prostheses employing the same are disclosed, wherein the composite material may be formulated into a fluid injectable, **gel** or rehydratable **freeze** dried paste. The resultant **products** can be used either alone or combined with a prosthetic device as an osteoinductive/osteoconductive material.

IT **9004-61-9, Hyaluronic acid**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. collagen, demineralized human bone powder and other substances for repair of defects in osseous tissue)

L30 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:515629 HCAPLUS

DOCUMENT NUMBER: 122:268527

TITLE: Effect of **preparation method** on

the hydration characteristics of hylan and comparison with another highly crosslinked polysaccharide, gum arabic

AUTHOR(S): Takigami, Shoji; Takigami, Michiko; Phillips, Glyn O.
 CORPORATE SOURCE: Dep. of Chemistry, Gunma Univ., Japan
 SOURCE: Carbohydrate Polymers (1995), 26(1), 11-18
 CODEN: CAPOD8; ISSN: 0144-8617

PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The water binding characteristics of hylan are compared with gum arabic (I) using DSC. Both polysaccharide systems bind water effectively, and the transitions characteristic of two types of **freezing**-bound water can be distinguished from the melting or **freezing** of free water. There is evidence for the existence of metastable states of **freezing**-bound water within the two systems. I binds considerably less **freezing**-bound water than hylan systems. I does not have the same ability as **hyaluronic acid** to form structured entangled networks which can incorporate water within the matrix. The hylan samples are of two types: hylan fluid where the hyaluronan chains are crosslinked with HCHO, and hylan **gel** where the crosslinking agent is vinyl sulfone. The hylan **gel** retains the **freezing**-bound state of water as a stable thermodyn. state .apprx.20-50% more effectively than hylan **prepd.** from the **freeze**-dried solid **prepd.** from either concd. or dil. hylan fluid. The traps formed from **freeze**-dried hylan **gel** are also more stable. Hylan **gel prepd.** by pptn. with iso-PROH and **freeze**-dried is the most effective hylan sample for stabilizing the **freezing** bound state. For this material even in .apprx.6% soln. the vast majority of the water is retained in the **freezing**-bound form.

L30 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:244780 HCAPLUS
 DOCUMENT NUMBER: 122:17138
 TITLE: Biological characterization of hydrogels of poly(vinyl alcohol) and **hyaluronic acid**

AUTHOR(S): Del Guerra, R. Sbarbati; Cascone, M. G.; Barbani, N.; Lazzeri, L.
 CORPORATE SOURCE: C.N.R. Inst. Fisiologia Clinica, Pisa, Italy, 56126, Italy
 SOURCE: Journal of Materials Science: Materials in Medicine (1994), 5(9&10), 613-16
 CODEN: JSMREL; ISSN: 0957-4530

PUBLISHER: Chapman & Hall
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Hydrogels of **hyaluronic acid** (HA) and poly(vinyl alc.) (PVA) were **prepd.** using 8 **freezing-thawing** cycles from HA/PVA blends (10/90, 20/80, 30/70, 40/60, 50/50, and 0/100, wt./wt. ratios). The biocompatibility of the hydrogels was tested by means of in vitro cytotoxicity and cytocompatibility tests using cell culture **techniques**. The release with time of HA and PVA, the 2 hydrogel components, in aq. medium was also monitored and evaluated. The results indicate that all the hydrogels are not cytotoxic, while cell adhesion was very scarce in PVA and was not improved by the addn. of HA. The release kinetics of HA and PVA from the hydrogels were different. After 2 h, HA percentages from about 80 (10/90 blend) to 100% (20/80,

40/60 blends) were released from the hydrogels into the aqs. medium. In contrast, the percentages of released PVA remain lower in time compared with HA, reaching a plateau after 24 h and ranging from a max. of about 13% (0/100 blend) to a min. of about 6% (10/90, and 20/80 blends).

IT **9004-61-9, Hyaluronic acid**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxicity and cytocompatibility of hydrogels of poly(vinyl alc.)
and **hyaluronic acid**)

L30 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:418087 HCAPLUS

DOCUMENT NUMBER: 121:18087

TITLE: **Preparation** of microspheres of diagnostic agents

INVENTOR(S): Sutton, Andrew Derek; Johnson, Richard Alan

PATENT ASSIGNEE(S): Delta Biotechnology Ltd., USA

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9408627 | A1 | 19940428 | WO 1993-GB2091 | 19931008 |
| W: CA, GB, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 663840 | A1 | 19950726 | EP 1993-922577 | 19931008 |
| GB 2286122 | A1 | 19950809 | GB 1995-7191 | 19931008 |
| GB 2286122 | B2 | 19970409 | | |
| JP 08505366 | T2 | 19960611 | JP 1993-509745 | 19931008 |
| GB 2302649 | A1 | 19970129 | GB 1996-16116 | 19931008 |
| GB 2302649 | B2 | 19970409 | | |
| GB 2302650 | A1 | 19970129 | GB 1996-16117 | 19931008 |
| GB 2302650 | B2 | 19970409 | | |
| EP 1226832 | A2 | 20020731 | EP 2002-76722 | 19931008 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT, IE | | | | |
| US 6015546 | A | 20000118 | US 1995-465621 | 19950605 |
| US 6348186 | B1 | 20020219 | US 1995-465236 | 19950605 |
| US 6344182 | B1 | 20020205 | US 1995-411815 | 19950628 |
| US 6416741 | B1 | 20020709 | US 1999-390467 | 19990903 |

PRIORITY APPLN. INFO.:

| | | |
|----------------|----|----------|
| GB 1992-21329 | A | 19921010 |
| EP 1993-922577 | A3 | 19931008 |
| GB 1995-7191 | A3 | 19931008 |
| WO 1993-GB2091 | W | 19931008 |
| US 1995-465621 | A1 | 19950605 |
| US 1995-411815 | A1 | 19950628 |

AB Microspheres are **prepd.** by a **process** comprising the steps of (I) spray-drying a soln. or dispersion of a wall-forming material, e.g. albumin, in order to obtain intermediate microspheres and (II) reducing the water-soly. of at least the outside of the intermediate microspheres. The microsphere have walls of 40-500 nm thick and are useful in ultrasonic imaging. In particular, the microspheres may be 15-20 .mu.m, targeted to selected areas of the body or of prolonged life in the circulation. A soln. of 5% human albumin was spray-dried at temp. of 220.degree. and air pressure of 1.5 bar and the resulting particles were heat fixed for 20 min at 175.degree.. The samples were

deagglomerated by milling with mannitol and the particles were resuspended in a soln. of 10mg/mL mannitol and 0.06 mg/mL Pluronic F68. The intact particles were sepd. and the microsphere suspension was **freeze**-dried. Particles of 10-20.mu.m were produced which contained air and were substantially pressure resistant.

IT 9004-61-9, **Hyaluronic acid**
RL: BIOL (Biological study)
(pharmaceutical microspheres manuf. from, comprising diagnostic agents)

L30 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:420448 HCAPLUS

DOCUMENT NUMBER: 111:20448

TITLE: Ice crystal patterns in artificial **gels** of extracellular matrix macromolecules after quick-**freezing** and **freeze**-substitution

AUTHOR(S): Allenspach, Allan L.; Kraemer, Thomas G.

CORPORATE SOURCE: Dep. Zool., Miami Univ., Oxford, OH, 45056, USA

SOURCE: Cryobiology (1989), 26(2), 170-9

CODEN: CRYBAS; ISSN: 0011-2240

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Artificial **gels**, composed of collagen with or without hyaluronate (HA), a glycosaminoglycan (GAG), and chondroitin sulfate (CS), were **prepd.** and quick-frozen for the purpose of studying the influence of compn. and concn. on ice patterns. Dil. **gels** were spread on coverslips, plunged into a slush of 30% isopentane/70% propane (-185.degree.), **freeze**-substituted, and examd. by phase-contrast microscopy. Ice patterns were revealed as ice cavities in the **gel** after **freeze**-substitution. Ice morphol. in the **gels** was **gel**-type-specific, suggesting that compn. in dil. **gels** can influence ice pattern formation. Crystn. patterns reflecting high, intermediate, and low rates of **freezing** were obsd. in all **gel** types. Intermediate **freezing** velocities proved the most useful in differentiating **gel**-type-specific ice patterns. **Gels** which included by hyaluronate (HA) and chondroitin sulfate (CS) altered the ice crystal pattern commonly obsd. in collagen **gels**. Ice structure in collagen **gels** consisted predominantly of long, parallel crystals in the herringbone pattern. Ice crystals sepd. **gel** into thin, unbranched fibers with a primary spacing of .apprx.2 .mu.m. Ice morphol. in HA **gels** formed a mosaic consisting of packets of ice crystals. Contiguous packets were often oriented at right angles to each other. Periodic crossbridges interconnect primary **gel** fibers of HA **gels** and interrupt the lengthwise growth of ice crystals. Smooth beads were visible on primary strands in HA **gels** frozen at intermediate velocities. The addn. of CS to collagen **gels** resulted in formation of randomly oriented ice crystals in **gels** frozen at intermediate rates. CS has little influence on ice morphol. at low **freezing** velocities. Primary strands in CS **gels** were decorated with rough-surfaced, osmiophilic aggregates. Spacings between primary **gel** strands were not noticeably different (.ltoreq.2 .mu.m) in HA, CS, and std. **gels**. Ice crystals produced at intermediate **freezing** rates in extremely dil. **gels** form patterns that contribute to the understanding of the interaction of matrix constituents during the quick-**freezing** process.

IT 9004-61-9, **Hyaluronic acid**
RL: ANST (Analytical study)
(in artificial collagen **gel**, ice crystal patterns response)

to, after quick **freezing** and **freeze** substitution)

L30 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:121503 HCAPLUS

DOCUMENT NUMBER: 110:121503

TITLE: **Process** for forming multilayer
bioreplaceable blood vessel prosthesis from
crosslinked collagen-aminopolysaccharide reaction
products

INVENTOR(S): Yannas, Ioannis V.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA

SOURCE: U.S., 8 pp. Cont. of U.S. Ser. No. 369,614, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| US 4787900 | A | 19881129 | US 1987-3178 | 19870112 |
| PRIORITY APPLN. INFO.: | | | US 1982-369614 | 19820419 |

AB A blood vessel prosthesis comprises (1) a tubular nonporous inner layer that is 0.1-5 mm thick, has a smooth surface, and consists of a covalently crosslinked collagen-aminopolysaccharide reaction **product** that has a no.-av. mol. wt. between crosslinks of 5000-10,000, and (2) an outer layer which has a thickness of .gtoreq.1.0 mm and consists of a crosslinked collagen-aminopolysaccharide that has a no.-av. mol. wt. of 10,000-20,000 between crosslinks, a mean pore diam. of >50 .mu.m, and forms a porous, bioreplaceable outer surface. A dispersion of bovine hide collagen was **freeze**-dried, milled, and sieved through a 20-mesh screen, and the milled collagen (0.55 g) was placed in a blender, stirred at high speed, and mixed with a soln. contg. 0.44 g chondroitin 6-sulfate in 20 mL 0.5M AcOH. The dispersion was fed from a pressurized Plexiglas tank into a flow development module and into a perforated Al tube (0.03-in. pores) that was fitted lengthwise with filter paper; upon transport of H₂O and particles through the tube, a fraction of the H₂O and the dispersion was forced through the perforations in the tube wall, whereas the remainder of the dispersion was pumped back into the tank. At an applied pressure of 30 psig and a flow rate of 2.5 mL/min, a **gel** layer 0.004 in. thick had formed after 6 h; the tubular compn. was air dried, removed from the tubular mold without detachment from the filter paper, and crosslinked by immersion into a 0.5% wt./wt. glutaraldehyde soln. to give a tube with a wall thickness of 0.028-0.034 mm. The tube was mounted onto a Plexiglas mandrel, immersed in a pan contg. a dispersion of collagen-aminopolysaccharide, the pan was **freeze**-dried, and the spongy slab thus formed was removed and the material had a pore diam. of 80 .mu.m; the porous material was left attached to the inner nonporous cylinder, sufficient material was removed, the conduit was placed in an oven at 105.degree. and 50 millitorr for 24 h, and the mandrel was then placed in 0.5% wt./wt. glutaraldehyde soln. to effect crosslinking. The multilayered conduit was stored in the **freeze**-dried state in a sterile container contg. Me₂CHOH-H₂O (70:30).

IT **9004-61-9D, Hyaluronic acid, reaction**
products with collagen, crosslinked

RL: BIOL (Biological study)

(blood vessel prostheses contg. porous and nonporous layers of)

L30 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1987:571840 HCAPLUS

DOCUMENT NUMBER: 107:171840

TITLE: **Preparative** electrophoresis on agarose submerged **gels** of two aggregating proteoglycan monomers from articular cartilage

AUTHOR(S): Stanescu, Victor; Pham, Thuc Do

CORPORATE SOURCE: Unite Rech. Genet. Med., Hop. Enfants-Malades, Paris, 75743, Fr.

SOURCE: Preparative Biochemistry (1987), 17(3), 229-38
CODEN: PRBCBQ; ISSN: 0032-7484

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Anal. electrophoresis on polyacrylamide-agarose **gels** of aggregating proteoglycan monomers from baboon articular cartilage produces two distinct bands corresponding to 2 different aggregating monomer populations; a **preparative** electrophoresis **procedure** is described for isolated the monomers. Proteoglycans were extd. from young baboon articular cartilage in 4M guanidinium chloride contg. proteolysis inhibitors and aggregated after **hyaluronic acid** addn. The aggregates were sepd. from nonaggregated proteoglycans by isopycnic centrifugation, followed by **gel** chromatog. on Sepharose CL-2B. The monomers of the aggregates were obtained by isopycnic centrifugation under dissociative conditions. Two monomers were sepd. by **preparative** electrophoresis on 0.8% agarose submerged **gels**. Approx. 60% of the proteoglycans were recovered from the **gel** using a **freeze-squeeze procedure**. Aliquots of the sepd. monomers gave single bands when submitted to anal. polyacrylamide-agarose **gel** electrophoresis. Their migration and appearance were similar to that of the 2 bands present in the nonseparated **prepn.** of monomers.

L30 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1950:41055 HCAPLUS

DOCUMENT NUMBER: 44:41055

ORIGINAL REFERENCE NO.: 44:7917e-h

TITLE: Principles of isolation and some properties of the highly polymerized **hyaluronic acid**

AUTHOR(S): Shapot, V. S.; Kogan, L. S.

SOURCE: Doklady Akad. Nauk S.S.S.R. (1950), 70, 1041-4

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB After an investigation of the earlier **techniques**, the following **procedure** for isolation was evolved: The minced tissue (umbilical) is extd. with physiol. salt soln. and a small amt. of CHCl₃ and 1 vol. of centrifuged ext. is repeatedly treated with 3/5 vol. CHCl₃ and 1/20 vol. AmOH until a **gel** interface vanishes. The clear protein-free filtrate is pptd. by 2 vols. EtOH and the ppt. is washed progressively with 70-100% EtOH and dried in vacuo over P₂O₅; all operations are done in the cold at pH 7. The **product** is not pptd. by La indicating removal of nucleic acids. The threadlike **product** is easily sol. in H₂O, losing 25-30% of its wt. on vacuum drying at 110.degree. with corresponding loss of soly. and lowering of viscosity; the latter varies steeply with concn. (from 9 to 107, relative to H₂O, in 0.05-0.18% solns.) indicating a high order of mol. asymmetry. Presence of small amts. of inorg. salts depresses viscosity very sharply (10-11 times), with convergence of results for solns. of initially widely

different viscosities. This salt effect is reversed by dialysis. The pptd. fibers when freshly made are highly elastic and rubberlike.

=> d que stat 132

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L18      1 SEA FILE=REGISTRY ABB=ON  "HYALURONIC ACID"/CN
L19      12762 SEA FILE=HCAPLUS ABB=ON  L18 OR ?HYALURONIC?(W)?ACID?
L20      1653 SEA FILE=HCAPLUS ABB=ON  L19 AND GEL?
L21      857 SEA FILE=HCAPLUS ABB=ON  L20 AND (?PRODN? OR ?PRODUCT? OR
?PREP? OR ?SYNTH?)
L22      342 SEA FILE=HCAPLUS ABB=ON  L21 AND (?METHOD? OR ?PROCED? OR
?PROCES? OR ?TECHNIQ? OR ?TECHNIC? OR ?MECHANISM?)
L23      7 SEA FILE=HCAPLUS ABB=ON  L22 AND (?MEDIC?(W)?MATER?)
L24      25 SEA FILE=HCAPLUS ABB=ON  L22 AND (?FREEZ? OR ?THAW?)
L25      30 SEA FILE=HCAPLUS ABB=ON  L23 OR L24
L27      3 SEA FILE=HCAPLUS ABB=ON  L22 AND PH(L) 3.5
L28      32 SEA FILE=HCAPLUS ABB=ON  L25 OR L27
L29      2 SEA FILE=HCAPLUS ABB=ON  L22 AND ?BRANCH?(W)?DEGREE?
L30      32 SEA FILE=HCAPLUS ABB=ON  L28 OR L29
L31      39 SEA L30
L32      33 DUP REMOV L31 (6 DUPLICATES REMOVED)

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=> d ibib abs 132 1-33

L32 ANSWER 1 OF 33 MEDLINE

ACCESSION NUMBER: 2003049485 IN-PROCESS

DOCUMENT NUMBER: 22446417 PubMed ID: 12559822

TITLE: The properties of chitosan-**gelatin** membranes and scaffolds modified with **hyaluronic acid** by different **methods**.

AUTHOR: Mao Jin Shu; Liu Hai Feng; Yin Yu Ji; Yao Kang De
CORPORATE SOURCE: Research Institute of Polymeric Materials, Tianjin University, 300072, Tianjin, China.

SOURCE: BIOMATERIALS, (2003 Apr) 24 (9) 1621-9.
Journal code: 8100316. ISSN: 0142-9612.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20030202

Last Updated on STN: 20030202

AB The objective of the present study was to investigate the properties of chitosan-**gelatin** membranes or scaffolds, which were modified by incorporation of **hyaluronic acid** in the surface or bulk phase through co-crosslinking with N,N-(3-dimethylamino-propyl)-N'-ethyl carbodiimide (EDC) and N-hydroxysuccinimide (NHS) in 2-morpholinoethane sulfonic acid (MES) buffer. The comparative study on properties of surface modification (HA(S)) and polyblend membranes (HA(C)) revealed that **gelatin** was enriched on the surface of HA(C), while **hyaluronic acid** was enriched on the surface of the HA(S). The HA(S) membranes made by surface modification **method** had a characteristic surface morphology. The corresponding scaffolds were **prepared** through **freeze-drying**. The incorporation of **hyaluronic acid** improved flexibility and fibroblasts adhesion, while slowing down the rate of biodegradation of chitosan-**gelatin** scaffold. Human fibroblasts adhered and proliferated well on the membranes or scaffolds in vitro.

L32 ANSWER 2 OF 33 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2003-129498 [12] WPIDS

DOC. NO. CPI: C2003-033235

TITLE: Stable aqueous solution useful for producing
therapeutical liquid formulations and medicaments for
treating allergic diseases, comprises an antibody,
especially an anti-IgE antibody and an acidic component.

DERWENT CLASS: B04 D16

INVENTOR(S): ARVINTE, T; FAUQUEX, P F

PATENT ASSIGNEE(S): (GETH) GENENTECH INC; (NOVS) NOVARTIS AG; (NOVS)
NOVARTIS-ERFINDUNGEN VERW GES MBH

COUNTRY COUNT: 87

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|----------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2002096457 | A2 | 20021205 | (200312)* | EN | 37 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE TR | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK | | | | | |
| DM DZ EC EE ES FI GB GD GE GH HR HU ID IL IN IS JP KE KG KP KR KZ | | | | | |
| LC LK LT LU LV MA MD MK MN MX NO NZ OM PH PL PT RO RU SE SG SI SK | | | | | |
| TJ TM TN TR TT UA US UZ VN YU ZA ZW | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 2002096457 | A2 | WO 2002-EP6016 | 20020531 |

PRIORITY APPLN. INFO: GB 2001-13179 20010531

AN 2003-129498 [12] WPIDS

AB WO 200296457 A UPAB: 20030218

NOVELTY - A stable aqueous solution (I) comprising an antibody at a concentration of at least 50 mg/ml, and at least 1 acidic component, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) a nasal spray comprising (I);
- (2) a slow release formulation (II) comprising (I);
- (3) a delivery system which contains (I) chosen from single use injection syringes or inhalation devices;
- (4) use of an acidic component for the **preparation** of an aqueous solution comprising an antibody having a concentration of at least 50 mg/ml;
- (5) **preparing** (I), by admixing an antibody with an acidic component;
- (6) a therapeutical liquid formulation (III) **prepared** by employing (I); and
- (7) **preparation** of a therapeutical liquid formulation comprising an antibody, by adding an acidic component on the last purification step of the **preparation** of the antibody.

ACTIVITY - Antiallergic; Antiasthmatic; Antiparasitic; Dermatological.

No biological data given.

MECHANISM OF ACTION - Anti-IgE antibody therapy.

USE - (I) Is useful for producing a delivery system for the treatment of a disease, and in drying or **freeze drying process**.

(I) Is also useful in medicine, and in the manufacture of a medicament for the treatment of a disease, especially an allergic disease. (I) Is useful for **preparing** a therapeutical liquid formulation comprising an antibody at a concentration of more than 50 mg/ml. In the first step an

antibody solution in a suitable buffer is concentrated to a concentration of 10-50 mg/ml, in a second step, the concentrated solution is diafiltered with (I), optionally containing MgCl₂ and/or CaCl₂ and/or further suitable additives, and in a third step the solution obtained is further concentrated to a concentration of more than 50 mg/ml, or to an intermediate concentration of 100-200 mg/ml, preferably 100-150 mg/ml. Optionally in a fourth step, the intermediate concentrated solution is diafiltered with the aqueous solution and the solution obtained is further concentrated to more than 150 mg/ml. In between the third and fourth step a solution of MgCl₂ and/or CaCl₂ and/or further suitable additives are directly added to the intermediate concentrated solution obtained in the third step (claimed).

The allergic diseases include IgE-mediated allergic diseases, parasitic infections, interstitial cystitis and asthma, in particular allergic asthma, allergic rhinitis and atopic dermatitis.

ADVANTAGE - The aqueous solution has high stability, high protein concentration and low viscosity.

Dwg.0/0

L32 ANSWER 3 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 2002-682912 [73] WPIDS
 DOC. NO. NON-CPI: N2002-539136
 DOC. NO. CPI: C2002-192745
 TITLE: Elongated biopolymer structure e.g. thread useful for wound healing contains fibrin.
 DERWENT CLASS: B04 B07 D16 D22 F01 P34
 INVENTOR(S): DELMOTTE, Y; DELMOTTE, Y A
 PATENT ASSIGNEE(S): (DELM-I) DELMOTTE Y; (BAXT) BAXTER HEALTHCARE SA; (BAXT) BAXTER INT INC
 COUNTRY COUNT: 97
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2002070795 | A1 | 20020912 | (200273)* | EN | 64 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW | | | | | |
| US 2002168398 | A1 | 20021114 | (200277) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 2002070795 | A1 | WO 2002-EP2315 | 20020304 |
| US 2002168398 | A1 | US 2001-800070 | 20010306 |

PRIORITY APPLN. INFO: US 2001-800070 20010306

AN 2002-682912 [73] WPIDS

AB WO 200270795 A UPAB: 20021113

NOVELTY - An elongated biopolymer structure containing fibrin has at least a portion stretched in at least one direction.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) **preparation** of the biopolymer structure involving mixing a fibrinogen-containing material (a) with a substance (b) having the capability of converting fibrinogen to fibrin;
 (2) an article comprising the structure; and
 (3) **process** (P1) for manufacturing a shaped article involving mixing an aqueous fibrinogen-containing solution with thrombin in an active form. The amount of water in the solution is such that after activation of the thrombin and polymerization of the material into a **gel**, no water can be removed when the **gel** is centrifuged at 1000 rounds per minute.

ACTIVITY - Vulnerary.

No suitable biological data given.

MECHANISM OF ACTION - None given in source material.

USE - The articles comprising the structure include e.g. thread, tube, hollow profile, film, fleece, sponge or membrane (claimed). The articles are useful for directing wound healing and cell growth especially in the field of tissue engineering.

Dwg.0/14

L32 ANSWER 4 OF 33 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2002-691631 [74] WPIDS

CROSS REFERENCE: 2001-529174 [58]; 2001-549795 [61]; 2002-065947 [09]

DOC. NO. NON-CPI: N2002-545624

DOC. NO. CPI: C2002-195478

TITLE: Mixing syringe for reconstituting paste, comprises barrel containing midsection having flexible portion which is compressible by hand for mixing syringe contents, and plunger.

DERWENT CLASS: A96 B04 B07 D22 P32

INVENTOR(S): BERNHARDT, A; KAO, P; WALPOLE, M; WIRONEN, J F

PATENT ASSIGNEE(S): (REGE-N) REGENERATION TECHNOLOGIES INC

COUNTRY COUNT: 95

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2002067814 | A2 | 20020906 | (200274)* | EN | 36 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ | | | | | |
| NL OA PT SD SE SL SZ TR TZ UG ZM ZW | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK | | | | | |
| DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ | | | | | |
| LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD | | | | | |
| SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 2002067814 | A2 | WO 2002-US5903 | 20020226 |

PRIORITY APPLN. INFO: US 2001-976556 20011011; US 2001-792894 20010226

AN 2002-691631 [74] WPIDS

CR 2001-529174 [58]; 2001-549795 [61]; 2002-065947 [09]

AB WO 200267814 A UPAB: 20021118

NOVELTY - A mixing syringe (1100) comprises a barrel (1110) and a plunger (1105), adapted for insertion into the barrel at the second end. The

midsection of the barrel comprises a flexible portion such that the portion is compressible by hand, and the contents of the syringe are mixed upon compression of the midsection.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) A **method** of mixing two or more substances which involves disposing the substances into the mixing syringe and squeezing the midsection of the mixing syringe;

(2) An article of manufacture comprising a mixing syringe and at least one biomedical substance further disposed in the mixing syringe;

(3) A **method** of repairing a bone defect, injury or deformation which involves disposing paste component(s) in the mixing syringe, storing paste component in the mixing syringe for at least 24 hours, subsequently disposing an amount of reconstitution fluid into the mixing syringe, squeezing the flexible portion of the mixing syringe such that the at least one paste component and reconstitution fluid are mixed to form a mixture, and extruding the mixture to a site of need, by removing a portion of barrel;

(4) A dried paste composition comprising **freeze-dried** demineralized bone matrix (DBM) particles and a carrier. The carrier is **gelatin, hyaluronic acid**, polyethylene oxide, chondroitin sulfate, polyvinyl pyrrolidone, polyvinyl alcohol, collagen and/or dextran; and

(5) A reconstituted paste composition comprising a mixture of a dried paste composition and reconstitution fluid.

USE - For reconstituting bone paste, and/or other biochemical paste or powders.

ADVANTAGE - The dried paste composition upon reconstitution possesses osteogenic, chondrogenic and/or chondroprotective properties. The system allows for a more expeditious and facile use and **preparation** of pastes. The bone paste, and/or other biomedical pastes or powders, are reconstituted in decreased time at low costs and inefficiencies associated with their storage. The **method** pertains to a storing **method** for bone pastes that provides long-shelf life and simple implementation of the stored bone paste. The **method** cuts down on the costs of preserving bone and/or other biomedical pastes, and extends their shelf life. The dried paste compositions are capable of being stored at room temperature and retaining their osteogenic, chondrogenic, or chondroprotective properties upon reconstitution.

DESCRIPTION OF DRAWING(S) - The figure shows

Mixing syringe 1100

Plunger 1105

Barrel 1110

Dwg.11/14

L32 ANSWER 5 OF 33 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2002-691472 [74] WPIDS

DOC. NO. NON-CPI: N2002-545566

DOC. NO. CPI: C2002-195336

TITLE: Substrate for tissue regeneration comprises **hyaluronic acid** or derivative sponge and polymer materials derived from living bodies laminated on the sponge as tissue connection part.

DERWENT CLASS: B04 D22 P34

INVENTOR(S): KUROYANAGI, Y

PATENT ASSIGNEE(S): (NITI-N) JAPAN TISSUE ENG CO LTD; (KURO-I) KUROYANAGI Y

COUNTRY COUNT: 98

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2002045767 | A1 | 20020613 | (200274)* | JA | 35 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2002021089 | A | 20020618 | (200274) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|-----------------|----------|
| WO 2002045767 | A1 | WO 2001-JP10751 | 20011207 |
| AU 2002021089 | A | AU 2002-21089 | 20011207 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|------------|--------------|
| AU 2002021089 | A Based on | WO 200245767 |

PRIORITY APPLN. INFO: JP 2000-373116 20001207

AN 2002-691472 [74] WPIDS

AB WO 200245767 A UPAB: 20021118

NOVELTY - A substrate for tissue regeneration comprises a **hyaluronic acid** and/or derivative sponge and a tissue connecting part laminated on the sponge and comprising a polymer material derived from a living body.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for

(1) **preparation** of the material by crosslinking the molecules of **hyaluronic acid** and/or derivative, forming a sponge by vacuum **freezing**, and laminating the tissue connecting part by absorbing polymer solution and then **freeze drying**;

(2) a similar **method** wherein the **hyaluronic acid** and/or derivative is contacted with a fabric while being crosslinked; and

(3) a transplant material using the substrate.

ACTIVITY - Vulnerary.

MECHANISM OF ACTION - None given.

USE - Used in skin graft, and transplant.

ADVANTAGE - The substrate has good affinity to living bodies.

DESCRIPTION OF DRAWING(S) - The drawing illustrates the **preparation**. The drawing contains non-English text.
Dwg.1/4

L32 ANSWER 6 OF 33 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2002-314931 [35] WPIDS

DOC. NO. CPI: C2002-091544

TITLE: **Preparation of konjac glucomannan gel**
or sponge, for e.g. the food industry, comprises making a sol by dispersing the gum in water, removing insoluble particulates, recovering the gum, drying, grinding to powder and dissolving in water.

DERWENT CLASS: B04 D16
 INVENTOR(S): BLAKE, N A; RENN, D W
 PATENT ASSIGNEE(S): (BLAK-I) BLAKE N A; (RENN-I) RENN D W; (MARI-N) MARINE
 BIOPRODUCTS INT
 COUNTRY COUNT: 100
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------|----|----|
| US 2002019447 | A1 | 20020214 | (200235)* | | 31 |
| WO 2002072687 | A2 | 20020919 | (200263) | EN | |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|-----------|----------------|----------|
| US 2002019447 | A1 CIP of | US 2000-609870 | 20000703 |
| | | US 2001-804402 | 20010313 |
| WO 2002072687 | A2 | WO 2002-CA334 | 20020311 |

PRIORITY APPLN. INFO: US 2001-804402 20010313; US 2000-609870
 20000703

AN 2002-314931 [35] WPIDS

AB US2002019447 A UPAB: 20020603

NOVELTY - **Production** of a clarified konjac glucomannan (A) **gel** or sponge, clarified konjac glucomannan or clarified aloe mannan (B) film, foam or capsule by soaking dispersed (A) or (B) in water, stirring to obtain a homogenous particulate containing sol, removing insoluble particulates, recovering (A) or (B), drying and grinding to a powder, dissolving the powder in water and forming into a required form.

DETAILED DESCRIPTION - **Production** of a clarified konjac glucomannan (A) **gel** or sponge, or a clarified aloe mannan (B) film, foam, capsule, **gel** or sponge by:

(a) soaking dispersed (A) or (B) in water, stirring the hydrated (A) or (B) until a homogenous particulate containing sol is obtained, removing insoluble particulates, recovering clarified (A) or (B) from the filtrate, drying and grinding to a powder, and optionally dissolving the powder in water to form a sol; where

(b) **preparation** of (A) **gel** involves adding a suitable alkaline agent to a sol of the clarified (A) of step (a) to deacetylate the sol to form the **gel**;

(c) **preparation** of (A) flexible water soluble film involves adding glycerol or other plasticizer to a sol of the clarified (A) or (B) of step (a), dissolving (A) or (B), glycerol or other plasticizer mixture, casting the mixture as a film, and drying the film;

(d) **preparation** of (A) flexible hot water soluble film involves adding xanthan and glycerol or other plasticizer to the clarified sol of (A) or (B) of step (a) to form a mixture, dissolving the mixture, casting the mixture as a film, cooling the film to a **gel** and drying the **gel** to form the film;

(e) **preparation** of (A) flexible water-insoluble film involves adding glycerol or other plasticizer and an alkaline agent to the clarified sol of (A) of step (a) to form a mixture, dissolving the mixture, casting the mixture as a sol, heating the sol to deacetylate the mixture to form a **gel** and drying the **gel** to form the film;

(f) **preparation** of (A) rigid water soluble film involves step (c) but omitting the glycerol or other plasticizer;

(g) **preparation** of (A) rigid hot water soluble film involves step (d) but omitting the glycerol or other plasticizer;

(h) **preparation** of (A) rigid water insoluble film involves step (e) but omitting the glycerol or other plasticizer;

(i) **preparation** of (A) in the form of the water-inhibiting film that forms an amorphous **gel** involves adding an appropriate amount of glycerol and borax to the clarified (A) or (B) of step (a), dissolving the mixture, casting the mixture as a film and drying the film;

(j) **preparation** of (A) stabilized foam involves adding a foaming agent and glycerol to the clarified sol of (A) step (a) to form a mixture, aerating the mixture to produce a foam, adding an alkaline agent to the foam, heating the foam to set the foam and drying the foam;

(k) **preparation** of (A) flexible rubbery type foam involves adding a foaming agent, clarified xanthan and glycerol or other plasticizer to the clarified sol of (A) or (B) in step (a) to form a mixture, heating the mixture to form a sol, aerating the mixture to produce a foam, cooling the foam to set the foam, and drying the foam;

(l) when a sponge cloth-like foam is required, following step (j), but before drying the foam, **freezing** and **thawing** the foam, squeezing the foam, rinsing the foam, soaking the foam in isopropyl alcohol and drying the foam;

(m) **preparation** of (A) flexible, dry foam which rehydrates to form an amorphous **gel** involves adding a detergent and glycerin or other plasticizer to the sol of (A) of step (a) to form a mixture, aerating the mixture to form a foam, adding a borate to the foam, aerating the foam further, cooling and then drying the foam;

(n) **preparation** of (A) firm water absorbent sponge involves adding an alkaline agent to a sol of the clarified (A) of step (a) to form a mixture, heating the mixture until a **gel** is formed, **freezing** the **gelled** mixture, **thawing** the **gelled** mixture, and drying the **gelled** mixture; and

(o) **preparation** of (A) flexible water absorbent sponge involves step (n) but before drying and after **thawing** the sponge, soaking the sponge in isopropyl alcohol containing a suitable plasticizer, squeezing and drying the sponge.

INDEPENDENT CLAIMS are also included for the following:

(1) **production** of a clarified hydrocolloid guar gum (C) or locust bean gum (D), **gel**, film, foam or capsule;

(2) borating a cis-1,2-diol containing hydrocolloid;

(3) **preparation** of a capsule of clarified hydrocolloid;

(4) **production** of a reduced viscosity clarified sol of (A);

(5) **production** of a hydrocolloid composite containing at least two hydrocolloids which when hydrated, forms a clear hydrocolloid composite sol;

(6) a clarified hydrocolloid composite that forms a clear sol when mixed with water that is a clarified konjac and clarified (C), clarified konjac and clarified xanthan gum, clarified xanthan gum and clarified (C), clarified (B) and clarified (C), clarified konjac and clarified agar, clarified (B) and clarified konjac, clarified konjac and clarified (D), clarified konjac and clarified carboxymethyl cellulose, or clarified (C)

and clarified carboxymethyl cellulose;

(7) **preparation** of a capsule of clarified composite hydrocolloid (preferably clarified guar, agar **gel** composite of (C) and xanthan **gel**; agar and (A); (A) and xanthan **gel**; hydrogen peroxide induced low-viscosity (A) and xanthan **gel**; or (C) and xanthan **gel**).

USE - The **method** is used for the **production** of clarified polysaccharide sols, particularly sols of konjac glucomannan, aloe mannan, guar gum, locust bean gum for the **production** of **gels**, sponge, films, foams, capsules clarified composite hydrocolloids (claimed), in food, pharmaceutical and cosmetic industries.

ADVANTAGE - The **method** is simple, cost-effective and results in dry hydrocolloid **products** that, when reconstituted, form clear viscous sols, free of all particulates and retain desirable physical properties, unlike the commercially available **products**.
Dwg.0/6

L32 ANSWER 7 OF 33 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-529791 [57] WPIDS
DOC. NO. NON-CPI: N2002-419563
DOC. NO. CPI: C2002-150007
TITLE: **Process for preparing dual-layer combined chitosan-gelatin-mucilage scaffold material.**
DERWENT CLASS: A96 D16 P73
INVENTOR(S): MAO, J; YAO, K; YIN, Y
PATENT ASSIGNEE(S): (UYTI-N) UNIV TIANJIN
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|------------|------|----------|-----------|----|----|
| CN 1342722 | A | 20020403 | (200257)* | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|------------|------|----------------|----------|
| CN 1342722 | A | CN 2001-141966 | 20010926 |

PRIORITY APPLN. INFO: CN 2001-141966 20010926

AN 2002-529791 [57] WPIDS

AB CN 1342722 A UPAB: 20020906

NOVELTY - A dual-layer combined chitosan-gelatin-hyaluronic acid scaffold material is **prepared** through dissolving chitosan/gelatin in acetic acid, adding the aqueous solution of **hyaluronic acid**, adding carbodiimide cross-linking agent, pouring in a mould, pre-freezing at -20-200 deg. C, vacuum **freeze**-drying at -40 deg. C and under 5KPa, and secondary **freeze**-drying. It can be used for culture of different cells.
Dwg.0/0

L32 ANSWER 8 OF 33 JICST-EPlus COPYRIGHT 2003 JST
ACCESSION NUMBER: 1020863313 JICST-EPlus
TITLE: Research on the material which is excellent in biocompatibility and functionality and development of the

evaluation technology (human science promotion foundation
S).

AUTHOR: TSUCHIYA TOSHIE; NAKAOKA RYUSUKE
MASUDA SHIGEKI
KATAKURA TAKEO
ASO YU
IMAYASU MASAKI
IKEDA HIROYUKI
KARIYA YUTAKA

CORPORATE SOURCE: National Inst. Health Sciences, JPN
Kaneka Corp., JPN
Terumo Corp., JPN
Koken Co., Ltd., Baiosaiensu Kenkyusho
Menikon Soken
Ube Ind., Ltd., Chiba Lab., JPN
Seikagakukogyochuoken

SOURCE: Soyakuto Hyuman Saiensu Kenkyu Juten Kenkyu Hokokusho.
Heisei 13 Nendo. Dai6 Bun'ya. Iyo Zairyo oyobi Seizai
Sekkei Gijutsu no Kaihatsu ni kansuru Kenkyu, (2002) pp.
20-34. Journal Code: N20022139 (Fig. 7, Tbl. 1, Ref. 17)

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Short Communication

LANGUAGE: Japanese

STATUS: New

AB In the interaction with the bFGF on the connexin function, that the effect in which the heparin derivative with the desulphation completely contradicts enhancement and control of the connexin function on the specific position of heparin by the difference between the position of the sulfate group was shown clarified. It was clarified that dynamic stimulation and addition of physical strength maintenance constituent like the **hyaluronic acid** were influential **methods** in order to make bio salve which shows the fixed and dynamic strength. The dynamic evaluation system equipment for creating the bio salve which is excellent in the biocompatibility was left up. Three-dimensional matrix structure body of the multiple kind was produced. It was proven that the functionality was very high for chondroitin sulfate derivative with the moderate fucose junction in plasminogen activator evaluation test through the t-PA. The rabbit anterior epithelium of the cornea cell three-dimensional culture body which was similar to the form of invitro anterior epithelium of the cornea was able to be produced. By neutralizing the atelocollagen under the optimal condition, various honeycomb fragments were able to be produced. The evaluation **method** was established, when it was denatured using collagen - **gelatine** which was denatured in the system diversity, and the invivo evaluation was carried out. As the result, the effect on a vital reaction is different by the denatured state.

L32 ANSWER 9 OF 33 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2002-216781 [27] WPIDS

DOC. NO. CPI: C2002-066189

TITLE: **Preparation** of active enamel substance for **preparation** of a composition for formation or regeneration of dentin following dental **procedures** comprising exposure of vital dental pulp tissue.

DERWENT CLASS: A96 B04 D21

INVENTOR(S): GESTRELIUS, S; LYNGSTADAAS, S P

PATENT ASSIGNEE(S): (BIOR-N) BIORA BIOEX AB

COUNTRY COUNT: 96

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2001097834 | A1 | 20011227 | (200227)* | EN | 59 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2001074374 | A | 20020102 | (200230) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 2001097834 | A1 | WO 2001-IB1076 | 20010620 |
| AU 2001074374 | A | AU 2001-74374 | 20010620 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|------------|--------------|
| AU 2001074374 | A Based on | WO 200197834 |

PRIORITY APPLN. INFO: DK 2000-1665 20001108; DK 2000-959
20000620; US 2000-213790P 20000623

AN 2002-216781 [27] WPIDS

AB WO 200197834 A UPAB: 20020429

NOVELTY - **Preparation** of an active enamel substance (I) for the **preparation** of a pharmaceutical composition for the formation or regeneration of dentin following dental **procedures** involving exposure of vital dental pulp tissue.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a **method** of promoting the formation or regeneration of dentin following dental **procedures** comprising exposure of vital dental pulp tissue, and applying active enamel substance on exposed vital dental pulp tissue after dental pulp tissue after dental **procedures**.

ACTIVITY - None given.

MECHANISM OF ACTION - Dentin formation/regeneration promoter (claimed).

Six adult (18 months of age or older) Gottingen minipigs were anesthetized with Dormicum and also locally anesthetized by injection of Xylocain and adrenalin. The pulps of permanent maxillary premolars and molars (a total of 36 teeth) were exposed in buccal class V cavities using a sterilized round steel burr with saline spray. The most coronal part of the pulp was then removed to make a pulp wound of with an area of more than 2 mm².

The vitality of the pulp was demonstrated by abundant bleeding that was brought under control using sterile cotton pellets. After bleeding had stopped, an enamel matrix derivative (EMD) or calcium hydroxide (Ca(OH)₂) paste as control, were applied directly onto the exposed pulp.

The cavities were then sealed with a glass ionomer filling in a **procedure** mimicking ordinary clinical situations. After two or four weeks, the animals were sacrificed and the experimental teeth were extracted and embedded in paraffin, and histological sections were stained

with hematoxylin and eosin.

Microscopy of the histological sections revealed a thick dentin-like closure of the pulp chamber adjacent to the filling material after four weeks in the location where EMD had been applied. In controls without EMD no or only rudimentary dentin formation was observed and none of the control teeth exhibited complete closures of the pulp chamber.

USE - (I) is useful for the **preparation** of a pharmaceutical composition for the formation or regeneration of dentin following dental **procedures** comprising exposure of vital dental pulp tissue.

(I) is useful for regeneration of secondary dentin in vital dental pulp tissue, for the formation of reparative dentin or osteodentin in vital dental pulp tissue, and for promoting dentin formation in vital dental pulp tissue in erupted teeth.

(I) is useful for promoting the formation or regeneration of dentin following dental **procedures** involving exposure of vital dental pulp tissue, by applying an effective amount of (I) on exposed vital dental pulp tissue after dental **procedures**, where the application of (I) is followed by application of a filling material (claimed). (I), preferably the enamel matrix derivative is useful for direct pulp capping **procedure**.

ADVANTAGE - (I) possesses bioadhesive properties, i.e. it has the ability to adhere firmly to tissue surfaces, and this property is valuable in connection with endodontic treatment because they ensure a fast and intimate contact between enamel matrix proteins and the dentin-producing odontoblasts so as to facilitate the **process** of dental root regeneration.

Dwg.0/13

L32 ANSWER 10 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 2002-105969 [14] WPIDS
 DOC. NO. CPI: C2002-032452
 TITLE: Delivery system useful for topical application to skin
 e.g. in the treatment of wrinkles, comprises a
freeze-dried, partially cross-linked polymeric
gel membrane which can be reversibly returned to
 a dissolvable **gel** form.
 DERWENT CLASS: A96 B05 B07 D16 D21
 INVENTOR(S): CASTILLO-BUCCI, C; KNIGHT, E A; ZECCHINO, J
 PATENT ASSIGNEE(S): (COLO-N) COLOR ACCESS INC
 COUNTRY COUNT: 24
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|----------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2001078692 | A2 | 20011025 | (200214)* | EN | 15 |
| RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR | | | | | |
| W: AU CA JP | | | | | |
| AU 2001051548 | A | 20011030 | (200219) | | |
| US 6497887 | B1 | 20021224 | (200303) | | |
| EP 1276471 | A2 | 20030122 | (200308) | EN | |
| R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|-----------------|----------|
| WO 2001078692 | A2 | WO 2001-US11876 | 20010411 |
| AU 2001051548 | A | AU 2001-51548 | 20010411 |

US 6497887 B1
EP 1276471 A2

US 2000-549113 20000413
EP 2001-924942 20010411
WO 2001-US11876 20010411

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|--------------|
| AU 2001051548 | A Based on | WO 200178692 |
| EP 1276471 | A2 Based on | WO 200178692 |

PRIORITY APPLN. INFO: US 2000-549113 20000413

AN 2002-105969 [14] WPIDS

AB WO 200178692 A UPAB: 20020301

NOVELTY - A delivery system for topical application to the skin comprises:

- (1) a **freeze**-dried, partially cross-linked polymeric **gel** membrane which can be reversibly returned to a dissolvable **gel** form upon the application of
- (2) a wetting agent.

DETAILED DESCRIPTION - INDEPENDENT CLAIM is included for a kit for delivery of a biologically active agent to the skin and comprising (1) and (2) for it.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - None given.

USE - For topical application to the skin (claimed); in treatments including delivering active compounds such as moisturizers and skin conditioning agents for stretching, smoothing, tightening and re-moisturizing the skin, particularly the skin with fine lines and wrinkles; anti-acne compounds; agents for treating chrono or photoaging; whitening agents for treating age spots, freckles and skin discolorations associated with hormonal changes in localized treatment; and hormones such as estrogen or progesterone.

ADVANTAGE - The application pieces of the membrane delivery system are convenient to use, easier to carry and store compared to the traditional vehicles used for delivery of actives to the skin such as lotions and creams in bottles and jars; and other types of patches. Like other patch-type **products**, the **gel** membrane can retain on the skin for prolonged periods, and therefore permits sustained delivery of the actives to the skin; however, unlike other skin patches and films, the re-wetted membrane need not have to be peeled or washed off after use, but simply dissolves and is rubbed into the skin. Thus provides immediate benefits by the rubbing in of the **gel** right after application and wetting, and avoids the potentially unattractive appearance of the patch in a highly visible locations such as the face. The membrane also serves as a stabilizer for the active ingredients. This is due to the fact that as the application pieces are maintained in a dry state until used, active ingredients that are normally affected by the presence of water, or other environmental factors e.g. retinoids, greentea, polyphenols, enzymes or vitamin C, retain their activity even after prolonged periods of storage, and hence such compounds which have to be specially formulated or delivered in special packaging in order to retain their activity before the **product** reaches the consumer, can be rendered stable in simple and relatively inexpensive manner. Thus the topical delivery system is more convenient to use and more elegant, than the prior art delivery forms and devices, while at the same time retains the efficacy of providing the desired actives to the target location.

Dwg.0/0

L32 ANSWER 11 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 2001-581724 [65] WPIDS
 DOC. NO. NON-CPI: N2001-433396
 DOC. NO. CPI: C2001-172397
 TITLE: **Preparation of hyaluronic acid gel**, comprises adding an acid ingredient to **hyaluronic acid** and water.
 DERWENT CLASS: A11 D22 P34
 INVENTOR(S): ARAI, K; KANEKO, H; KAWATA, M; KITAGAWA, H; MIYATA, Y; MIYOSHI, T; OHSHIMA, K; OKAMOTO, A; UMEDA, T; YAMAMOTO, O
 PATENT ASSIGNEE(S): (ELED) DENKI KAGAKU KOGYO KK
 COUNTRY COUNT: 90
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2001057093 | A1 | 20010809 | (200165)* | JA | 42 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2000023250 | A | 20010814 | (200173) | | |
| EP 1281722 | A1 | 20030205 | (200310) | EN | |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 2001057093 | A1 | WO 2000-JP582 | 20000203 |
| AU 2000023250 | A | AU 2000-23250 | 20000203 |
| | | WO 2000-JP582 | 20000203 |
| EP 1281722 | A1 | EP 2000-902065 | 20000203 |
| | | WO 2000-JP582 | 20000203 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|--------------|
| AU 2000023250 | A Based on | WO 200157093 |
| EP 1281722 | A1 Based on | WO 200157093 |

PRIORITY APPLN. INFO: WO 2000-JP582 20000203

AN 2001-581724 [65] WPIDS

AB WO 200157093 A UPAB: 20011108

NOVELTY - **Preparation of hyaluronic acid gel** comprises adding an acid ingredient to a mixture of at least 5 weight% **hyaluronic acid** and water in an amount of at least mole equivalent to the carboxy groups of **hyaluronic acid**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(i) a transparent **hyaluronic acid gel** comprising poorly soluble **hyaluronic acid** in aqueous

solution; and

(ii) a **medical material** comprising:

(a) the above **gel** which has less than 50% solubility in water at 25 deg. C over 1 day; or

(b) a transparent **gel** consisting of **hyaluronic acid**.

USE - As a **gel** useful as a **medical material** e.g. for injection into diseased joints, as a shaped stopper, as a soft textured injectable agent and as a glass substitute.

ADVANTAGE - **Gel** is transparent and stable and it dissolves in water gradually, over a long period of time.

Dwg.0/0

L32 ANSWER 12 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 2001-182695 [18] WPIDS
 DOC. NO. NON-CPI: N2001-130462
 DOC. NO. CPI: C2001-054434
 TITLE: Forming anti-adhesion barrier, particularly for wounds, by **freeze-drying** solution of **hyaluronic acid** to form foam, reacting with crosslinking agent and mixing with aqueous solution containing **hyaluronic acid**.
 DERWENT CLASS: A96 B07 P32
 INVENTOR(S): ZHANG, G
 PATENT ASSIGNEE(S): (USSU) US SURGICAL CORP; (ZHAN-I) ZHANG G
 COUNTRY COUNT: 30
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|----------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2001006973 | A1 | 20010201 | (200118)* | EN | 26 |
| RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE | | | | | |
| W: AU CA JP MX US | | | | | |
| AU 2000076267 | A | 20010213 | (200128) | | |
| EP 1207828 | A1 | 20020529 | (200243) | EN | |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT | | | | | |
| RO SE SI | | | | | |
| US 2002141968 | A1 | 20021003 | (200267) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|-----------------|--------------------------|
| WO 2001006973 | A1 | WO 2000-US40491 | 20000726 |
| AU 2000076267 | A | AU 2000-76267 | 20000726 |
| EP 1207828 | A1 | EP 2000-965568 | 20000726 |
| | | WO 2000-US40491 | 20000726 |
| US 2002141968 | A1 | Provisional | US 1999-146065P 19990728 |
| | | | US 2001-36239 20011228 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|--------------|
| AU 2000076267 | A Based on | WO 200106973 |
| EP 1207828 | A1 Based on | WO 200106973 |

PRIORITY APPLN. INFO: US 1999-146065P 19990728

AN 2001-182695 [18] WPIDS
AB WO 200106973 A UPAB: 20010402
NOVELTY - Forming an anti-adhesion barrier comprises:
(a) **freeze**-drying a solution including **hyaluronic acid** (HA) to form a foam;
(b) reacting the foam with a crosslinking agent to form a crosslinked foam and
(c) mixing the crosslinked foam with an aqueous solution containing HA to form an anti-adhesion barrier.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an anti-adhesion barrier which is a **gel** produced by combining **freeze**-dried crosslinked HA foam with an aqueous solution comprising HA;

(2) a 2-part kit comprising a first part including a **freeze**-dried crosslinked HA foam and a second part including a solution including HA and

(3) an anti-adhesion barrier comprising a HA foam, a crosslinking agent and an aqueous solution containing HA.

ACTIVITY - Vulnerary.

MECHANISM OF ACTION - None given.

USE - Used as an anti-adhesion barrier for preventing or inhibiting the formation of adhesions at a wound site and for promoting healing of a wound. The barrier can be used to inhibit adhesions that form in relation to intestinal surgery e.g. bowel resection or hernia repair, which may cause obstruction of the intestine. The barrier may also prevent or inhibit adhesions that form near a bone fracture site which may reduce or hinder the normal movement of the area of repair by restricting the natural movement of tendons over adjacent bone.

ADVANTAGE - The **method** eliminates the concern of low solubility of HA in various solvents. The crosslinking agents only react with those functional groups accessible on surfaces, so that the use of a **freeze**-dried HA foam provides a relatively large surface area containing sites for crosslinking. The **production** of crosslinked HA foam results in a near-quantitative recovery of crosslinked HA foam. The excess crosslinking agent and any reaction by-products can be easily removed by simple washing.
Dwg.0/2

L32 ANSWER 13 OF 33 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-112499 [12] WPIDS
CROSS REFERENCE: 2001-091751 [10]
DOC. NO. CPI: C2001-033517
TITLE: **Method** for controlling the flux of penetrants across an adaptable semi-permeable barrier is useful for administering an agent to a mammalian body or a plant and for generating an immune response by vaccinating the mammal.
DERWENT CLASS: A18 A28 A96 B05 B07 D16 D22
INVENTOR(S): CEVC, G; RICHARDSEN, H; WEILAND-WAIBEL, A;
WEILAND-WEIBEL, A
PATENT ASSIGNEE(S): (IDEA-N) IDEA AG
COUNTRY COUNT: 95
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|----------|-----------|----|-----|
| ----- | | | | | |
| WO 2001001963 | A1 | 20010111 | (200112)* | EN | 110 |

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000061557 A 20010122 (200125)
 BR 2000012178 A 20020312 (200226)
 EP 1189598 A1 20020327 (200229) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 CZ 2002000038 A3 20020515 (200241)
 CN 1359288 A 20020717 (200268)
 HU 2002001454 A2 20021228 (200308)
 JP 2003503442 W 20030128 (200309) 109

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 2001001963 | A1 | WO 2000-EP6367 | 20000705 |
| AU 2000061557 | A | AU 2000-61557 | 20000705 |
| BR 2000012178 | A | BR 2000-12178 | 20000705 |
| | | WO 2000-EP6367 | 20000705 |
| EP 1189598 | A1 | EP 2000-947939 | 20000705 |
| | | WO 2000-EP6367 | 20000705 |
| CZ 2002000038 | A3 | WO 2000-EP6367 | 20000705 |
| | | CZ 2002-38 | 20000705 |
| CN 1359288 | A | CN 2000-809916 | 20000705 |
| HU 2002001454 | A2 | WO 2000-EP6367 | 20000705 |
| | | HU 2002-1454 | 20000705 |
| JP 2003503442 | W | WO 2000-EP6367 | 20000705 |
| | | JP 2001-507458 | 20000705 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|--------------|
| AU 2000061557 | A Based on | WO 200101963 |
| BR 2000012178 | A Based on | WO 200101963 |
| EP 1189598 | A1 Based on | WO 200101963 |
| CZ 2002000038 | A3 Based on | WO 200101963 |
| HU 2002001454 | A2 Based on | WO 200101963 |
| JP 2003503442 | W Based on | WO 200101963 |

PRIORITY APPLN. INFO: WO 1999-EP4659 19990705

AN 2001-112499 [12] WPIDS

CR 2001-091751 [10]

AB WO 200101963 A UPAB: 20030206

NOVELTY - A **method** for controlling the flux of penetrants across an adaptable semi-permeable porous barrier is new.

DETAILED DESCRIPTION - A **method** for controlling the flux of penetrants across an adaptable semi-permeable membrane comprises suspending the penetrants in a polar liquid in the form of fluid droplets surrounded by a membrane-like coating comprising at least two kinds of amphiphilic substances with a tendency to aggregate, selecting a dose of the penetrants to control the flux of the penetrants across the barrier and applying the selected dose of the formulation onto the area of the

barrier. The amphiphilic substances differ by a factor of at least 10 in solubility in the polar liquid and the homo-aggregates of the more soluble substance and hetero-aggregates have a preferred average diameter smaller than the diameter of the homo-aggregates of the less soluble substance. The more soluble substance tends to solubilize the droplet and comprises up to 99% of the solubilizing concentration or saturating concentration in the unstabilized droplet. The presence of the more soluble substance lowers the average elastic energy of the coating by at least 5 times preferably more than 10 times the average elastic energy of red blood cells or of phospholipid bilayers with fluid aliphatic chains. The penetrants are able to transport agents through the pores of the barrier or enable agent permeation through the pores after the penetrants have entered the pores.

INDEPENDENT CLAIMS are included for:

- (i) a kit containing the formulation;
- (ii) a patch containing the formulation; and
- (iii) a **method** of administering an agent to a mammalian

body or plant comprising the novel **method**.

USE - The **method** is useful for administering an agent to a mammalian body or a plant, for generating an immune response by vaccinating the mammal and for treating inflammatory disease, dermatosis, kidney or liver failure, adrenal insufficiency, aspiration syndrome, Behcet syndrome, bites and stings, blood disorders (cold-hemagglutinin disease), hemolytic anaemia, hypereosinophilic, hypoplastic anaemia, macroglobulinaemia and thrombocytopenic purpura), bone disorders, cerebral oedema, Cogan's syndrome, congenital adrenal hyperplasia, connective tissue disorders (lichen, lupus erythematosus, polymyalgia rheumatica, polymyositis and dermatomyositis), epilepsy, eye disorders (cataracts), Graves' ophthalmopathy, hemangioma, herpes infections, neuropathies, retinal vasculitis, scleritis, gastro-intestinal disorders (inflammatory bowel disease, nausea and oesophageal damage), hypercalcaemia, infections, Kawasaki disease, myasthenia gravis, pain syndromes, polyneuropathies, pancreatitis, respiratory disorders (asthma), rheumatoid disease, osteoarthritis, rhinitis, sarcoidosis, skin diseases, alopecia, eczema, erythema multiforme, lichen, pemphigus and pemphigoid, psoriasis, pyoderma gangrenosum, urticaria and thyroid and vascular disorders.

ADVANTAGE - Increasing the applied dose above a threshold level affects both the drug/penetrant distribution and also determines the rate of penetrant transport across the barrier.

Dwg.0/14

| | | | |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|-------------|
| L32 | ANSWER 14 OF 33 | MEDLINE | DUPLICATE 1 |
| ACCESSION NUMBER: | 2001664893 | MEDLINE | |
| DOCUMENT NUMBER: | 21567274 | PubMed ID: 11710042 | |
| TITLE: | Thermoresponsive artificial extracellular matrix for tissue engineering: hyaluronic acid bioconjugated with poly(N-isopropylacrylamide) grafts. | | |
| AUTHOR: | Ohya S; Nakayama Y; Matsuda T | | |
| CORPORATE SOURCE: | Department of Bioengineering, National Cardiovascular Center Research Institute, Suita, Osaka 565-8565, Japan. | | |
| SOURCE: | Biomacromolecules, (2001 Fall) 2 (3) 856-63. Journal code: 100892849. ISSN: 1525-7797. | | |
| PUB. COUNTRY: | United States | | |
| DOCUMENT TYPE: | Journal; Article; (JOURNAL ARTICLE) | | |
| LANGUAGE: | English | | |
| FILE SEGMENT: | Priority Journals | | |
| ENTRY MONTH: | 200201 | | |
| ENTRY DATE: | Entered STN: 20011119 | | |

Last Updated on STN: 20020125

Entered Medline: 20020122

AB Thermoresponsive hyaluronans (HAs) were **prepared** by graft polymerization of N-isopropylacrylamide (NIPAM) on HA (number-averaged molecular weight, M_n , ca. 1.5×10^5 and 5.0×10^5) using dithiocarbamate which is a kind of iniferter (initiator, transfer agent and terminator). The degree of dithiocarbamylation (DD) as an iniferter ranged from 0.4 to 11.4% per disaccharide unit of HA. The estimated M_n of the grafted polyNIPAM (PNIPAM) ranged from approximately 5.0×10^3 to 8.4×10^4 . The PNIPAM-grafted HAs (PNIPAM-HAs) were water-soluble at room temperature, while they precipitated at temperatures above approximately 34 degrees C in water. The temperature at the onset of precipitation (lower critical solution temperature: LCST) was independent of parameters of molecular architecture such as M_n of HA, degree of grafting of PNIPAM, and M_n of PNIPAM. Equilibrium transmittance of the aqueous solution above LCST decreased with an increase in both degree of grafting and M_n of PNIPAM. At physiological temperature, the PNIPAM-HA film cast from a cold solution was very wettable with water. A markedly reduced adhesion of endothelial cells to the film was observed, indicating that the PNIPAM-HA film may serve as a non-cell-adhesive matrix. Scanning electron microscopic observation appeared to differentiate supramolecular structures between rapidly **freeze**-dried PNIPAM-HA and nongrafted HA: PNIPAM-HA exhibited a nonuniform fibrous network, whereas the morphology of which is markedly different from that of a nongrafted HA **gel** exhibited a mixture of sharp needle- and platelike structures.

L32 ANSWER 15 OF 33 MEDLINE DUPLICATE 2
 ACCESSION NUMBER: 2002025620 MEDLINE
 DOCUMENT NUMBER: 21366706 PubMed ID: 11475330
 TITLE: Hyaluronan molecular weight and polydispersity in some commercial intra-articular injectable **preparations** and in synovial fluid.
 AUTHOR: Adam N; Ghosh P
 CORPORATE SOURCE: Institute of Bone and Joint Research, Department of Surgery, University of Sydney, Royal North Shore Hospital, St. Leonards, NSW, Australia.
 SOURCE: INFLAMMATION RESEARCH, (2001 Jun) 50 (6) 294-9.
 Journal code: 9508160. ISSN: 1023-3830.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200112
 ENTRY DATE: Entered STN: 20020121
 Last Updated on STN: 20020121
 Entered Medline: 20011207

AB OBJECTIVE AND DESIGN: Hyaluronan is the major non-proteinaceous component of joint synovial fluid and is responsible for the unique rheological and biological properties of this medium. In joint arthropathies the molecular weight and concentration of hyaluronan may change, thereby influencing joint physiology and function. Intra-articular administrated hyaluronan derived from a number of sources, has been used for the treatment of osteoarthritis, however, there is limited information on the molecular weight and polydispersity of these various commercial **preparations**. The objective of this study was to develop an accurate, convenient **method** by which the molecular weight and polydispersity of hyaluronan may be determined and then applied to characterise the hyaluronan in synovial fluid. MATERIALS AND **METHODS**:

Characterisation of the molecular parameters of hyaluronan of different origins and in ovine synovial fluid was accomplished using a multi-angle laser-light scattering (MALLS) detector coupled to a **gel** permeation chromatography (GPC) system, fitted with an automatic sample injector. CONCLUSION: Seven commercially available hyaluronan **preparations** of reported molecular weight were analysed. The weight average molecular weight (Mw) and number average molecular weight (Mn) values obtained for 6 of the 7 **preparations** using the MALLS-GPC system were in good agreement with the reported values. The abnormally low values for the exception suggested that degradation of hyaluronan had occurred. The MALLS-GPC **technique** was then used to determine the molecular characteristics of the endogenous hyaluronan in normal ovine synovial fluids. While the Mws ranged from less than 1×10^6 Da to 7×10^6 Da the majority were between $1-3 \times 10^6$ Da. [mean Mw = 2.42×10^6 , mean Mn = 2.21×10^6 Da]. The effects of **freezing** and **thawing** synovial fluid upon molecular weight of hyaluronan were also investigated and were found to diminish both Mz and Mw values.

L32 ANSWER 16 OF 33 JICST-EPlus COPYRIGHT 2003 JST

ACCESSION NUMBER: 1020094349 JICST-EPlus
 TITLE: Friction and Wear Properties of PVA hydrogel.
 AUTHOR: NAKASHIMA KAZUHIRO; MURAKAMI TERUO; SAWAE YOSHINORI
 CORPORATE SOURCE: Kyushu Univ., Graduate School of Engineering, JPN
 SOURCE: Nippon Rinsho Baiomekanikusu Gakkaishi (Proceedings of Annual Meeting of Japanese Society for Orthopaedic Biomechanics), (2001) vol. 22, pp. 135-139. Journal Code: X0647A (Fig. 6, Tbl. 1, Ref. 4)
 ISSN: 1340-9018
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Conference; Article
 LANGUAGE: Japanese
 STATUS: New

AB Although the use of total joint replacements has become widespread particularly for diseased hip and knee joints, in certain cases, serious tribological problems such as loosening and wear has been reported. In this study, friction and wear in artificial cartilage material was evaluated in order to improve the fluid film formation between the articulating surfaces and reduce wear and friction by effective soft elastohydrodynamic lubrication(EHL). Polyvinyl Alcohol (PVA) hydrogel was used as the artificial cartilage material. It is known that the properties of PVA hydrogel produced by the **freezing-thawing method** can be controlled by the number of repetition for **freezing-thawing** cycles. Therefore, the influence of changes in material properties on tribological behavior was investigated by changing the **process** of **production**. Tribological properties of the artificial cartilage materials were examined in reciprocating test, in which a spherical zirconia ceramic was used as the upper specimen and the artificial cartilage material was used as the lower specimen. The reciprocating test was conducted in thin film lubrication under test conditions using different lubricants. After the test the artificial cartilage materials were observed by optical microscopy. Wear on rubbed surface was evaluated using 5 grades by comparison with the intact surface structure. The different repeating number of **freezing-thawing** cycles changed the elastic modulus and fracture stress of PVA hydrogel in tensile test and wear grade. Wear grade also changed according to the lubricants. The lubricant containing **hyaluronic acid** and protein reduced the coefficient of

friction and wear. (author abst.)

L32 ANSWER 17 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:385917 BIOSIS

DOCUMENT NUMBER: PREV200000385917

TITLE: Photocured cross-linked-hyaluronic acid
gel and method of preparation
thereof.

AUTHOR(S): Waki, Michinori (1); Miyamoto, Kenji

CORPORATE SOURCE: (1) Tokyo Japan

ASSIGNEE: Seikagaku Corporation, Tokyo, Japan

PATENT INFORMATION: US 6031017 February 29, 2000

SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (Feb. 29, 2000) Vol. 1231, No. 5, pp. No
pagination. e-file.
ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

AB A photocured crosslinked-hyaluronic acid gel
, which has a storage modulus (G') of from 50 to 1500 Pa, a loss modulus
(G'') of from 10 to 300 Pa, and a tangent delta (G''/G') of from 0.1 to 0.8
in dynamic viscoelasticity at a frequency of 10 Hz, and which is a
hydrogel obtained by irradiation with ultraviolet rays of a photoreactive
hyaluronic acid derivative in which a photoreactive
crosslinking group is chemically linked to a functional group of the
hyaluronic acid and crosslinking of mutual photoreactive
crosslinking groups, methods for preparing the same,
and uses thereof as biomedical materials.

L32 ANSWER 18 OF 33 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2000-587379 [55] WPIDS

DOC. NO. CPI: C2000-175194

TITLE: Preparing a pharmaceutical composition for
selective induction of apoptosis in neoplastic cells, and
for treating cancer, comprises using a
preparation of active enamel substance.

DERWENT CLASS: B04 D16 D21 D22

INVENTOR(S): GESTRELIUS, S; HAMMARSTROEM, L; LYGSTADAAS, S L P;
LYGSTADAAS, S P

PATENT ASSIGNEE(S): (BIOR-N) BIORA BIOEX AB

COUNTRY COUNT: 92

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 2000053196 | A1 | 20000914 | (200055)* | EN | 36 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL | | | | | |
| OA PT SD SE SL SZ TZ UG ZW | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE | | | | | |
| ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR | | | | | |
| LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK | | | | | |
| SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2000028210 | A | 20000928 | (200067) | | |
| EP 1162985 | A1 | 20011219 | (200206) | EN | |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT | | | | | |
| RO SE SI | | | | | |
| JP 2002538211 | W | 20021112 | (200275) | | 41 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 2000053196 | A1 | WO 2000-IB245 | 20000309 |
| AU 2000028210 | A | AU 2000-28210 | 20000309 |
| EP 1162985 | A1 | EP 2000-906552 | 20000309 |
| | | WO 2000-IB245 | 20000309 |
| JP 2002538211 | W | JP 2000-603685 | 20000309 |
| | | WO 2000-IB245 | 20000309 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|--------------|
| AU 2000028210 | A Based on | WO 200053196 |
| EP 1162985 | A1 Based on | WO 200053196 |
| JP 2002538211 | W Based on | WO 200053196 |

PRIORITY APPLN. INFO: DK 1999-336 19990310

AN 2000-587379 [55] WPIDS

AB WO 200053196 A UPAB: 20001102

NOVELTY - **Preparing** a pharmaceutical composition for the (selective) induction of apoptosis, and for prevention or treatment of malignant or benign neoplasms, and cancer, using a **preparation** (P) of an active enamel substance (I).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) inducing apoptosis in neoplastic cells comprising applying an effective amount of an active enamel substance at or on neoplastic cells; and

(2) preventing or treating malignant or benign neoplasms comprising administering an active enamel substance.

ACTIVITY - Cytostatic. No suitable biological data is given.

MECHANISM OF ACTION - Apoptosis inducer. The biological activity of enamel matrix derivative EMDOGAIN (RTM) containing 30 mg **freeze**-dried enamel matrix protein (EMD) and 1 ml vehicle solution (propylene glycol alginate) was tested in vitro. Human epithelial cells (HeLa; human cervical cancer cells) were grown in culture for 24, 48, 72, 96 and 120 hours. Cultures were then washed with phosphate buffered saline (PBS) and cells were counted in the microscope using a fixed grid. Five different areas were counted in each of six parallel cultures at each time point. The results showed that HeLa cells had a marked decrease in cell density from 48 hours when grown in the presence of EMD. HeLa cells were cultured for 24 or 120 hours, washed twice with PBS and centrifuged. 100 micro l of cells from each culture (n=6 at each time point/experiment) were then lysed, and released intracellular cAMP was measured by competitive enzyme immunoassay (EIA). HeLa cells show a marked increase in intracellular cAMP after 24 hours of growth in the presence of EMD. This increase could still be observed after 120 hours in culture. The increase in intracellular cAMP suggests that cells grown in the presence of EMD generate internal signal(s) that could be part of pathways for growth regulation and differentiation. HeLa cells were harvested from cultures at 24, 48, 72, 96 and 120 hours (n=5 at each time point/experiment), washed in PBS and centrifuged. 200 micro l cells were lysed, and the level of apoptosis specific nucleic acid degradation **products** was quantified by sandwich ELISA (enzyme linked immunosorbent assay). The results show a marked increase in induced cell death when EMD is present

in the cultures (values above 1), peaking at 72 hours after addition of EMD. Based on these results, it is concluded that epithelial cell growth is poorer in the presence of EMD, and that the presence of EMD in the cultures increased programmed cell death more than two-fold.

USE - (I) is useful for selectively inducing apoptosis in neoplastic cells, for preventing or treating malignant or benign neoplasms, in the topical treatment of epithelially derived cancer or neoplasms, and for reducing the risk of post-surgical metastasis or to substantially prevent recurrence of the tumor on application at or on a tumor site before, during or after a tumor operation (claimed).

ADVANTAGE - (P) comprising (I) can be applied for adjuvant cancer therapy e.g., in conjunction with conventional radiation therapy which may both reduce the risk of tumor cell migration and contribute to the healing of wounds often resulting from radiation therapy as (I) has also been found to exhibit wound healing properties.

Dwg.0/3

L32 ANSWER 19 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 2000-641881 [62] WPIDS
 DOC. NO. CPI: C2000-193901
 TITLE: Biocompatible base material for cell growth, for artificial skin and artificial organs comprises sparingly soluble **gel** of **hyaluronic acid** in neutral aqueous solution.
 DERWENT CLASS: B04 D16 D22
 PATENT ASSIGNEE(S): (ELED) DENKI KAGAKU KOGYO KK
 COUNTRY COUNT: 1
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|----------|-----------|----|----|
| JP 2000239304 | A | 20000905 | (200062)* | | 6 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|---------------|----------|
| JP 2000239304 | A | JP 1999-43286 | 19990222 |

PRIORITY APPLN. INFO: JP 1999-43286 19990222

AN 2000-641881 [62] WPIDS

AB JP2000239304 A UPAB: 20001130

NOVELTY - A base material for cell growth contains a sparingly soluble **gel** formed by **hyaluronic acid** in neutral aqueous solution.

USE - As biocompatible material for artificial skin (claimed) and artificial organs. Also for treatment of skin wounds by burns or ulcer and for treatment of damaged mucous membranes of oral cavity, by auto-transplantation using the base material.

ADVANTAGE - Since the cell growth base material is not using a cross-linking agent, it excels in safety, biocompatibility and enables cell growth inside or on the surface of base material. Thus the base material effectively acts as a medium for **production** of biologically useful substances by cell culture.

Dwg.0/0

L32 ANSWER 20 OF 33 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2000-368390 [32] WPIDS
 DOC. NO. CPI: C2000-111432
 TITLE: Sterile compositions comprising therapeutic peptides for topical administration, especially to the surface of a wound.
 DERWENT CLASS: B04 P34
 INVENTOR(S): CULLEN, B; HARVEY, W; SILCOCK, D; VANLEEUEWEN, P; VAN LEEUEWEN, P
 PATENT ASSIGNEE(S): (JOHJ) JOHNSON & JOHNSON MEDICAL LTD
 COUNTRY COUNT: 91
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------------------------------------------------------------------|------|----------|-----------|----|----|
| GB 2344519 | A | 20000614 | (200032)* | | 19 |
| WO 2000033893 | A1 | 20000615 | (200035) | EN | |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL | | | | | |
| OA PT SD SE SL SZ TZ UG ZW | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES | | | | | |
| FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS | | | | | |
| LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL | | | | | |
| TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2000015770 | A | 20000626 | (200045) | | |
| BR 9907679 | A | 20001024 | (200058) | | |
| EP 1053029 | A1 | 20001122 | (200061) | EN | |
| R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE | | | | | |
| CN 1290180 | A | 20010404 | (200140) | | |
| KR 2001040687 | A | 20010515 | (200167) | | |
| JP 2002531532 | W | 20020924 | (200278) | | 41 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| GB 2344519 | A | GB 1998-26897 | 19981207 |
| WO 2000033893 | A1 | WO 1999-GB4094 | 19991206 |
| AU 2000015770 | A | AU 2000-15770 | 19991206 |
| BR 9907679 | A | BR 1999-7679 | 19991206 |
| | | WO 1999-GB4094 | 19991206 |
| EP 1053029 | A1 | EP 1999-958396 | 19991206 |
| | | WO 1999-GB4094 | 19991206 |
| CN 1290180 | A | CN 1999-802742 | 19991206 |
| KR 2001040687 | A | KR 2000-708565 | 20000804 |
| JP 2002531532 | W | WO 1999-GB4094 | 19991206 |
| | | JP 2000-586383 | 19991206 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|--------------|
| AU 2000015770 | A Based on | WO 200033893 |
| BR 9907679 | A Based on | WO 200033893 |
| EP 1053029 | A1 Based on | WO 200033893 |
| JP 2002531532 | W Based on | WO 200033893 |

PRIORITY APPLN. INFO: GB 1998-26897 19981207
 AN 2000-368390 [32] WPIDS
 AB GB 2344519 A UPAB: 20000706

NOVELTY - A sterile composition (I) comprising a therapeutic peptide (TP) complexed to a biopolymer (BP) (the TP and BP are dispersed in or on a carrier), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a **process** (II) for the **preparation** of (I), comprising:

- (1) providing a complex of a TP and a BP;
- (2) sterilizing the complex; and
- (3) dispersing the complex in or on the carrier.

USE - (I) is a sterile composition that may be used for topically administering TPs to animals. It is particularly suitable for topically delivering these TPs to the skin, especially wound sites.

ADVANTAGE - The compositions (I) may be sterilized prior to administration as the TPs are stabilized against decomposition during sterilization by being formulated with a BP such as a structural protein or polyanionic polysaccharide.

Dwg.0/2

L32 ANSWER 21 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 2000-136890 [12] WPIDS
 DOC. NO. NON-CPI: N2000-102354
 DOC. NO. CPI: C2000-041962
 TITLE: New three dimensional prosthesis in shape of body part useful for reconstruction of human or animal body parts including nose, nasal septum, pharynx and joints.
 DERWENT CLASS: A11 A14 A28 A96 B07 D16 D22 P34
 INVENTOR(S): CALLEGARO, L; PASTORELLO, A; RADICE, M
 PATENT ASSIGNEE(S): (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL
 COUNTRY COUNT: 87
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 9965534 | A1 | 19991223 | (200012)* | EN | 24 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW | | | | | |
| AU 9946115 | A | 20000105 | (200024) | | |
| EP 1087797 | A1 | 20010404 | (200120) | EN | |
| R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE | | | | | |
| IT 1300270 | B | 20000503 | (200206) | | |
| JP 2002518101 | W | 20020625 | (200243) | | 29 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 9965534 | A1 | WO 1999-EP4167 | 19990616 |
| AU 9946115 | A | AU 1999-46115 | 19990616 |
| EP 1087797 | A1 | EP 1999-929241 | 19990616 |
| | | WO 1999-EP4167 | 19990616 |
| IT 1300270 | B | IT 1998-PD149 | 19980617 |
| JP 2002518101 | W | WO 1999-EP4167 | 19990616 |
| | | JP 2000-554411 | 19990616 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---------------|------|----------|------------|
| AU 9946115 | A | Based on | WO 9965534 |
| EP 1087797 | A1 | Based on | WO 9965534 |
| JP 2002518101 | W | Based on | WO 9965534 |

PRIORITY APPLN. INFO: IT 1998-PD149 19980617

AN 2000-136890 [12] WPIDS

AB WO 9965534 A UPAB: 20000308

NOVELTY - A three dimensional (3D) prosthesis (I) in a body part shape comprises at least one 3D matrix with an essentially fibrous or porous structure, containing at least one **hyaluronic acid** derivative. The prosthesis contains at least two of the 3D matrixes, one incorporates and/or is adhered to the other matrices and optionally incorporates and/or adheres to a bidimensional perforated matrix.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a **process** for the **preparation** of a 3D prosthesis where the matrix is a 3D matrix with an essentially fibrous structure and incorporates a porous 3D matrix and comprises:

(a) lining a mold with a layer of nonwoven tissue comprising a **hyaluronic acid** derivative;

(b) impregnating the non woven tissue in the mold with an aqueous solution of a quaternary ammonium salt of **hyaluronic acid** or a **hyaluronic acid** derivative;

(c) **freeze**-drying the content of the mold therefore obtaining a prostheses having a matrix A1 incorporating the matrix B consisting of the ammonium salts;

(d) optionally converting the ammonium salt contained in the prostheses coming from step (c) into a **hyaluronic acid** ; and

(e) **freeze**-drying the **product** from (c); and

(2) a **process** for **preparing** (I) where the matrix is an essentially porous 3D matrix or is the **product** of step (c) or (d) of (1) and is adhered to an essentially fibrous 3D matrix comprising:

(a) applying a thin layer of a solution of a **hyaluronic acid** derivative in a suitable aqueous or organic solvent;

(b) applying to the **freeze**-dried **product** from (a) a non-woven tissue comprising a **hyaluronic acid** derivative; and

(c) **freeze**-drying the **product** of (b).

USE - The three dimensional prosthesis (I) is useful for reconstruction of human or animal body parts e.g. nose, nasal septum, pharynx, larynx, joints, bone structures, eye socket, cardiac valves, blood vessels, nipple, navel, internal organs and their parts, the secondary sexual organs or especially auricula, knuckles or temporomandibular joint. (I) is useful in general, internal, otorhinolaryngological, plastic, aesthetic, oncological, orthopaedic, cardiovascular, gynecological and abdominal surgery and neurosurgery (all claimed). (I) is useful for acting as scaffolds for cell cultures. (I) is useful for the reconstruction of human or animal parts which have been damaged or are missing following trauma or as a result of congenital defects.

ADVANTAGE - The three dimensional prosthesis (I) is made easily into any form, however complex and according to the chemical structure of the **hyaluronic acid** derivative used and according to the

degree of esterification have the advantage of having tensile strength and degradation times that can be adjusted according to the requirement of the area to be reconstructed.

Dwg.0/0

L32 ANSWER 22 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1999-550865 [46] WPIDS
 DOC. NO. NON-CPI: N1999-407626
 DOC. NO. CPI: C1999-160646
 TITLE: **Preparation** of a living chimeric skin replacement.
 DERWENT CLASS: A25 A96 B04 D16 D22 P34
 INVENTOR(S): MANSBRIDGE, J N; NAUGHTON, G K; PINNEY, R E
 PATENT ASSIGNEE(S): (ADTI-N) ADVANCED TISSUE SCI INC
 COUNTRY COUNT: 84
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------|----|----|
| WO 9943787 | A2 | 19990902 | (199946)* | EN | 25 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW | | | | | |
| W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW | | | | | |
| AU 9933077 | A | 19990915 | (200004) | | |
| EP 1062322 | A2 | 20001227 | (200102) | EN | |
| R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE | | | | | |
| KR 2001072553 | A | 20010731 | (200209) | | |
| JP 2002504412 | W | 20020212 | (200215) | | 31 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 9943787 | A2 | WO 1999-US3859 | 19990223 |
| AU 9933077 | A | AU 1999-33077 | 19990223 |
| EP 1062322 | A2 | EP 1999-936092 | 19990223 |
| | | WO 1999-US3859 | 19990223 |
| KR 2001072553 | A | KR 2000-709299 | 20000823 |
| JP 2002504412 | W | WO 1999-US3859 | 19990223 |
| | | JP 2000-533527 | 19990223 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|------------|
| AU 9933077 | A Based on | WO 9943787 |
| EP 1062322 | A2 Based on | WO 9943787 |
| JP 2002504412 | W Based on | WO 9943787 |

PRIORITY APPLN. INFO: US 1998-75704P 19980224
 AN 1999-550865 [46] WPIDS
 AB WO 9943787 A UPAB: 19991110
 NOVELTY - A living chimeric skin replacement, is new.
 DETAILED DESCRIPTION - The **preparation** of a living chimeric skin replacement comprises:

(a) harvesting autologous epithelial cells from a patient; and
 (b) seeding them onto a biocompatible substrate containing allogeneic epithelial cells cultured in vitro.

INDEPENDENT CLAIMS are also included for the following:

(1) a **method** for making a chimeric skin replacement comprises the **preparation process** above;

(2) a **method** for implanting a chimeric skin replacement at a wound site, comprising:

(a) harvesting autologous epithelial cells from a patient; and either
 (b) seeding the autologous cells onto a biocompatible substrate containing allogeneic epithelial cells cultured in vitro to form a chimeric skin replacement and implanting the living chimeric skin replacement at the wound site by inverting the chimeric skin replacement so that the cells face into the wound site; or

(c) seeding the autologous epithelial cells into the wound site and implanting a biocompatible substrate containing allogeneic epithelial cells cultured in vitro into the wound site by inverting the substrate so that the allogeneic cells face inward toward the autologous cells;

(3) a composite skin replacement, having an inner, middle and outer component, comprising:

(a) an inner component comprising a biocompatible dermal construct having a biodegradable or removable scaffold as a base;

(b) a middle component comprising epithelial cells; and

(c) an outer component comprising epithelial cells cultured in vitro on a dermal construct comprising a dermal portion having a biodegradable or removable scaffold as a base, the dermal portion being combined with a transitional covering and facing inward toward the middle component of epithelial cells;

(4) a **method** of implanting a composite skin replacement of (3) into a wound site;

(5) a **method** for making a composite skin replacement in vivo at a wound site comprising:

(a) implanting an inner biocompatible first dermal construct having a biodegradable or removable scaffold as a base into the wound site;

(b) harvesting autologous epithelial cells from a patient;

(c) seeding the autologous epithelial cells on top of the inner dermal construct in the wound site; and

(d) implanting, on top of the autologous cells, an outer second dermal construct having epithelial cells cultured in vitro and comprising a dermal portion having a biodegradable or removable scaffold as a base, in combination with a transitional covering, so that the epithelial cells of the outer dermal construct face into the wound site; and

(6) a **method** for making a composite skin replacement in vitro, comprising:

(a) seeding epithelial cells on a first biocompatible dermal construct having a biodegradable or removable scaffold as a base; and

(b) placing a second dermal construct having epithelial cells cultured thereon and comprising a dermal portion having a biodegradable or removable scaffold as a base, in combination with a transitional covering, onto the first dermal construct, such that the cells of the second dermal construct face the cells on the first dermal construct.

ACTIVITY - Vulnerary.

MECHANISM OF ACTION - None given.

USE - The chimeric skin replacement is used where the wound site is a deep or full thickness wound, such as with burns.

Dwg.0/0

ACCESSION NUMBER: 1996-368085 [37] WPIDS
 DOC. NO. CPI: C1996-116223
 TITLE: Cosmetic materials with high moisture retention -
 contains polysaccharide comprising D-glucose,
 D-galactose, D-glucuronic acid, D-ribose and D-ribulonic
 acid.
 DERWENT CLASS: D16 D17 D21
 PATENT ASSIGNEE(S): (TKAK) TAYCA CORP
 COUNTRY COUNT: 1
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------|------|----------|-----------|----|----|
| JP 08175966 | A | 19960709 | (199637)* | | 9 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-------------|------|----------------|----------|
| JP 08175966 | A | JP 1994-339078 | 19941227 |

PRIORITY APPLN. INFO: JP 1994-339078 19941227

AN 1996-368085 [37] WPIDS

AB JP 08175966 A UPAB: 19960918

Cosmetic materials contain polysaccharide(s) having a mol. wt. of 1000-10000000 measured by **gel** filtration chromatography, comprising D-glucose, D-galactose, D-glucuronic acid, D-ribose and D-ribulonic acid with a glucose: galactose: glucuronic: ribose: ribulonic mol. ratio of 10: (1.8-2.9) : (1.8-2.6) : (0.5-1.7) : (0.5-1.7) , and a content of 0-acetyl gps. of 0-10 wt.%.
 EMBODIMENT - The polysaccharides are pref. acidic heteropolysaccharides and obtd. for Agrobacterium microorganisms. They are white fibrous (**freezing-dried prod**). soluble in water, dilute acid and alkali and DMSO and insol. in methanol, ethanol and acetone, have an absorption peak at 280 nm, characteristic of protein, and at 260 nm, characteristic of nucleic acid, in the UV absorption spectrum and absorption peaks about 3400, 2950, 1620, 1250 and 1110 cm⁻¹ in the IR absorption spectrum and undergo positive responses to phenol sulphurate, carbazole sulphate and m-phenyl phenol **methods**

ADVANTAGE - The materials have high moisture retention independent of variation of humidity conditions, compared with **hyaluronic acid**.
 Dwg.0/0

L32 ANSWER 24 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1995:261572 BIOSIS

DOCUMENT NUMBER: PREV199598275872

TITLE: Effect of **preparation method** on the hydration characteristics of hylan and comparison with another highly cross-linked polysaccharide, gum arabic.
 AUTHOR(S): Takigami, Shoji; Takigami, Michiko; Phillips, Glyn O. (1)
 CORPORATE SOURCE: (1) Newtech Innovation Cent., North East Wales Inst., Clwyd, Wales UK
 SOURCE: Carbohydrate Polymers, (1995) Vol. 26, No. 1, pp. 11-18. ISSN: 0144-8617.
 DOCUMENT TYPE: Article

LANGUAGE: English

AB The water binding characteristics of hylan are compared with another cross-linked polysaccharide Acacia senegal gum exudate (A. senegal) using differential scanning calorimetry. Both polysaccharide systems bind water effectively, and the transitions characteristic of two types of **freezing**-bound water can be distinguished from the melting or **freezing** of free water. There is evidence for the existence of metastable states of **freezing**-bound water within the two systems. Gum arabic binds considerably less **freezing**-bound water than hylan systems. A. senegal does not have the same ability as **hyaluronic acid** to form structured entangled networks which can incorporate water within the matrix. The hylan samples are of two types: hylan fluid where the hyaluronan chains are cross-linked with formaldehyde, and hylan **gel** where the cross-linking agent is vinyl sulphone. The hylan **gel** retains the **freezing**-bound state of water as a stable thermodynamic state ca 20-50% more effectively than hylan **prepared** from the **freeze**-dried solid **prepared** from either concentrated or dilute hylan fluid. The traps formed from **freeze**-dried hylan **gel** are also more stable. Hylan **gel prepared** by precipitation with isopropanol and **freeze**-dried is the most effective hylan sample for stabilizing the **freezing** bound state. For this material even in apprx 6% solution the vast majority of the water is retained in the **freezing**-bound form.

L32 ANSWER 25 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1988-051730 [08] WPIDS
 DOC. NO. CPI: C1988-022930
 TITLE: Glycose-amino-glycan degrading **prepn.s** contg.
 krill hyaluronidase - useful for degrading
hyaluronic acid and for treating
 myocardial infarction(s) and retinal functions, and with
 cytostatic agents.
 DERWENT CLASS: B04 D16
 INVENTOR(S): KARLSTAM, B E O; KARLSTAM, B
 PATENT ASSIGNEE(S): (KABI) KABI PHARMACIA AB; (PHAA) PHARMACIA AB
 COUNTRY COUNT: 15
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------------------------------------|------|----------|-----------|----|----|
| EP 257003 | A | 19880224 | (198808)* | EN | 7 |
| R: AT BE CH DE ES FR GB GR IT LI LU NL SE | | | | | |
| SE 8603051 | A | 19880110 | (198809) | | |
| JP 63024885 | A | 19880202 | (198810) | | |
| SE 456245 | B | 19880919 | (198840) | | |
| US 4904594 | A | 19900227 | (199015) | | 5 |
| EP 257003 | B1 | 19931013 | (199341) | EN | 9 |
| R: AT BE CH DE ES FR GB GR IT LI LU NL SE | | | | | |
| DE 3787773 | G | 19931118 | (199347) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-------------|------|----------------|----------|
| EP 257003 | A | EP 1987-850203 | 19870622 |
| JP 63024885 | A | JP 1987-170825 | 19870708 |
| US 4904594 | A | US 1987-65591 | 19870623 |

EP 257003 B1
DE 3787773 G

EP 1987-850203 19870622
DE 1987-3787773 19870622
EP 1987-850203 19870622

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|------------|------------|-----------|
| DE 3787773 | G Based on | EP 257003 |

PRIORITY APPLN. INFO: SE 1986-3051 19860709

AN 1988-051730 [08] WPIDS

AB EP 257003 A UPAB: 19931119

Glycosaminoglycan degrading enzyme **prepn.** contg. krill hyaluronidase isolated from appropriate organisms is claimed.

Prepns. are produced by homogenising animals of the order Euphausiaceae and extracting the homogenate with an aq. medium. The medium is then purified in respect to hyaluronidase activity, e.g. by affinity, gel or ion-exchange chromatography.

USE/ADVANTAGE - The **prepns.** can degrade **hyaluronic acid**, and may also be used as therapeutic agents, as they have positive effects on myocardial infarctions, on retinal function and in combination with cytostatic agents. Because of the degrading effect, the **prepns.** enhance the spreading of drugs through tissues. The **prepns.** have an activity over 2 units/mg proteins, esp. over 10 units/mg and even over 250 units/mg. The **prepn.** depolymerises **hyaluronic acid**, e.g. in a cell-free system, and stimulates **hyaluronic acid synthetase**, e.g. in cell culturing **procedures**.

Dwg.0/0

ABEQ US 4904594 A UPAB: 19930923

Glycosaminoglycan-degrading enzyme **prepn.** contains krill hyaluronidase isolated from organisms contg. them Hyaluronidase activity exceeds 10 U per mg of protein from source of raw material. **Prepn** . comprises extracting fresh krill or fresh-frozen krill which has been homogenised using water or other aq medium, then isolating enzyme by e g affinity gel or ion exchanges chromatography, PHLC, FPLC, chromatofocussing, **preperative** electrophoresis, dialysis, ultrafiltrations, or membrane sepn extn is at 4 deg C or less. Lipids are pref removed from crude extract.

ADVANTAGE - Materials used are inexpensive and have acceptable purity.

ABEQ EP 257003 B UPAB: 19931130

A glycosaminoglycan-degrading enzyme **preparation** containing hyaluronidase, characterised by said hyaluronidase being derived from krill and the activity of said hyaluronidase per mg of protein from the source of raw material being more than 25:3,4 times the same activity for a crude extract **prepared** from Euphausia superba that has been caught during the Antarctic summer, immediately frozen, stored at about -20 to -40 deg. C and **thawed** at +4 deg. C by (i) mixing 100 g of the **thawed** animals with 200 ml deionised water, (ii) homogenising to clearness, (iii) decanting and filtering the upper phase, (iv) treating the filtrate with three times the volume of a lipid-dissolving solvent, and (v) keeping the remaining aqueous as the crude extract, the protein being determined according to Lowry (8) using BSA as the reference protein and the hyaluronidase being determined according to Richman (12).

Dwg.0/0

L32 ANSWER 26 OF 33 JICST-EPlus COPYRIGHT 2003 JST

ACCESSION NUMBER: 890255811 JICST-EPlus
 TITLE: Light microscopic mucilaginous structures of human vitreous bodies embedded in the polyacrylamidgelfilm by toluidine blue staining.
 AUTHOR: HONDA SHIGEAKI
 CORPORATE SOURCE: Nagasaki Municipal Hospital
 SOURCE: Nagasaki Igakkai Zasshi (Nagasaki Medical Journal), (1988) vol. 63, no. 4, pp. 430-434, 434(1), 434(2). Journal Code: G0792A (Fig. 8, Ref. 6)
 CODEN: NAGZAC; ISSN: 0369-3228
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Journal; Article
 LANGUAGE: Japanese
 STATUS: New

AB Frozen sections were made from an eye of a 6 year-old boy which had to be enucleated caused by perforative eye injury, an eye from a 45 year-old female enucleated due to scleral staphyloma, an eye of a 67 year-old male died of subacute hepatitis, an adult bovine eye and Healon as a control. These frozen specimens were embedded in polyacrylamidgelfilms and stained by toluidine blue. The complex structure was observed from each specimens except that of Healon. These findings suggest that vitreous body has extremely complicated mucilaginous organisations. (author abst.)

L32 ANSWER 27 OF 33 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 87317409 MEDLINE
 DOCUMENT NUMBER: 87317409 PubMed ID: 3628196
 TITLE: **Preparative** electrophoresis on agarose submerged **gels** of two aggregating proteoglycan monomers from articular cartilage.
 AUTHOR: Stanescu V; Pham T D
 SOURCE: PREPARATIVE BIOCHEMISTRY, (1987) 17 (3) 229-38.
 Journal code: 1276634. ISSN: 0032-7484.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198710
 ENTRY DATE: Entered STN: 19900305
 Last Updated on STN: 19900305
 Entered Medline: 19871022

AB Analytical electrophoresis on polyacrylamide-agarose **gels** of aggregating proteoglycan monomers from baboon articular cartilage produces two distinct bands, corresponding to two different aggregating monomer populations. A **preparative** electrophoresis **procedure** is described for isolating the two monomers. Proteoglycans were extracted from young baboon articular cartilage in 4 M guanidinium chloride containing proteolysis inhibitors and aggregated after **hyaluronic acid** addition. The aggregates were separated from non-aggregated proteoglycans by isopycnic centrifugation, followed by **gel** chromatography on Sepharose CL-2B. The monomers of the aggregates were obtained by isopycnic centrifugation under dissociative conditions. Two monomers were separated by **preparative** electrophoresis on 0.8 % agarose submerged **gels**. Approximately 60 % of the proteoglycans were recovered from the **gel** using a **freeze-squeeze procedure**. Aliquots of the separated monomers gave single bands when submitted to analytical polyacrylamide-agarose **gel**

electrophoresis. Their migration and appearance were similar to that of the two bands present in the non separated **preparation** of monomers.

L32 ANSWER 28 OF 33 WPIDS (C) 2003 THOMSON DERWENT
 ACCESSION NUMBER: 1983-22693K [10] WPIDS
 DOC. NO. CPI: C1983-022162
 TITLE: Erythrogenic toxin isolation from streptococcus culture filtrates - by absorption on activated magnesium silicate at high ionic strength or low pH.
 DERWENT CLASS: B04 D16
 INVENTOR(S): GERLACH, D; KOEHLER, W
 PATENT ASSIGNEE(S): (DEAK) AKAD WISSENSCHAFTEN DDR
 COUNTRY COUNT: 1
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------|------|----------|-----------|----|----|
| DD 157243 | A | 19821027 | (198310)* | | 6 |

PRIORITY APPLN. INFO: DD 1981-228380 19810318

'AN 1983-22693K [10] WPIDS

AB DD 157243 A UPAB: 19930925

In the **prodn.** of erythrogenic toxins from Streptococcus cuo culture filtrates, (A) magnesium silicate is stirred into a fermented Streptococcal cultures (the cells optionally having been killed and/or removed) at high ionic strength (pref. 60g NaCl/litre) or at **pH** 3-6(pref. **3.5**); (B) the silicate-bound toxin is mechanically separated from the culture filtrate and the toxin seueluted by stirring with buffers at high **pH** (pref. 9.5-10) and precipitated with 500 g ammonium sulphate/litre; (C) the crude toxin, dissolved in water, is purified by twice absorbing on freshly **prepared** calcium phosphate **gel**, and concentrated with ammonium sulphate; and (D) further purification is effected by stepwise chromatography on cation-exchangers (pref. carboxymethyl-"Sephrose" (RTM)), abdsorption and washing being done at lwlow ionic strength (pref. 0.02- M acetate, **pH** 5.0) and elution at slightly higher ionic strength (pref. 0.05M, **pH** 5.2).

Simple **processs** suitable for large-scale use in the **prodn.** of highly purified toxin. The purification in quick and inexpensive, and **hyaluronic acid** is practically completely removed.

L32 ANSWER 29 OF 33 MEDLINE DUPLICATE 4
 ACCESSION NUMBER: 83147109 MEDLINE
 DOCUMENT NUMBER: 83147109 PubMed ID: 7164113
 TITLE: Purification and partial characterization of hyaluronidase from five pace snake (Agkistrodon acutus) venom.
 AUTHOR: Xu X; Wang X S; Xi X T; Liu J; Huang J T; Lu Z X
 SOURCE: TOXICON, (1982) 20 (6) 973-81.
 Journal code: 1307333. ISSN: 0041-0101.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198304

ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19980206
Entered Medline: 19830407

AB A hyaluronidase (EC 3.2.1. 35) was isolated and purified from Agkistrodon acutus venom. The purification **procedure** included CM-Sephadex C-50 chromatography, **gel**-filtration on Sephadex G-75 and CM-Sephadex C-25 chromatography. The purified **preparation** of the enzyme was homogeneous on polyacrylamide **gel** electrophoresis at **pH** 4.3, a 45-fold purification being obtained. The hyaluronidase was a glycoprotein (positive PAS staining) with a molecular weight of 33,000 and a pI of 10.3. No hemorrhagic activity was found. The hyaluronidase had an optimum **pH** of 3.5-5.0 and an optimum temperature of 37 degrees C. It was heat sensitive, was more stable in the acidic than in the neutral region, and lost its activity in the alkaline region. Fe²⁺, Cu²⁺ and heparin inhibited the venom hyaluronidase. The Km value for **hyaluronic acid** was 6.2 X 10⁽⁻³⁾ mg/ml.

L32 ANSWER 30 OF 33 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 77142812 EMBASE
DOCUMENT NUMBER: 1977142812
TITLE: Synovial cell activation induced by a polypeptide mediator.
AUTHOR: Castor C.W.
CORPORATE SOURCE: Dept. Int. Med., Univ. Michigan, Med. Sch., Ann Arbor, Mich. 48104, United States
SOURCE: Annals of the New York Academy of Sciences, (1975) Vol. 256/- (304-317).
CODEN: ANYAA
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
031 Arthritis and Rheumatism
LANGUAGE: English

AB Rheumatoid arthritis is exclusively a disease of man, and lack of an animal model has impeded progress in understanding its etiology and pathogenesis. In the synovial membrane, the **process** is characterized by intermittent connective tissue cell proliferation, **overproduction** of underpolymerized **hyaluronic acid**, increased glycolysis, exudation by inflammatory cells, and abnormalities of the microvasculature. In the hope of developing a relevant in vitro investigative model, 61 synovial cell strains from normal individuals and patients with different forms of arthritis were established. The 'abnormalities' detected in the rheumatoid cell strains (table) were propagated from one generation of cells to the next. Efforts to reproduce the 'rheumatoid' characteristics in normal synovial cells by adding rheumatoid sera to the media lead to minor and inconsistent alterations in cellular behavior. Because evidence for humoral factors capable of inducing 'rheumatoid behavior' in normal synovial cells was weak, the response of the normal cells to selected cellular factors was examined. Isolated human peripheral blood lymphocytes, granulocytes, and thrombocytes were cocultured with monolayer cultures of normal human synovial cells and found to cause profound changes in culture activity. These changes included decreased medium pH, marked acceleration of **hyaluronic acid synthesis**, and striking increases in glucose uptake and lactic acid formation. Slurries of dead leukocytes (frozen **thawed**) elicited the same hypermetabolic synovial cell response. Extracts of both syngeneic and allogeneic leukocytes stimulated synovial cells, and because of its protease lability, performance on **gel** permeation columns, and

nondialyzability, the active factor was thought to be a low molecular weight protein. The accelerated hyaluronate **synthesis**, and the increase in glucose uptake and lactate formation was termed 'connective tissue activation', and the cellular mediator(s) which initiate(s) this **process** was (were) named connective tissue activating peptide (CTAP). Major sources and actions of CTAP are summarized in a figure. The following are discussed separately in sequence: the isolation and characterization of CTAP; the assay of CTAP; the biologic significance of CTAP; the specificity of target cells and agonists; the inhibitors of synovial cell activation; and the **mechanism** of CTAP induced synovial cell activation. The locus of CTAP induced connective tissue activation is shown in a schematic drawing, at the junction of the exudative and reparative phases of simple inflammation. It is possible that other 'signals' may initiate cell proliferation, collagen **synthesis**, and so on. If simple inflammation is amplified by addition of immune reactions, the overall picture might show a simple sequence: injury.fwdarw.altered proteins.fwdarw.coagulation sequence.fwdarw.kinins etc..fwdarw.altered microcirculation.fwdarw.cellular exudation, phagocytosis.fwdarw.connective tissue activation.fwdarw.CTAP: CTAP causes increased energy metabolism, increase of cell proliferation, of hyaluronate formation, of collagen deposition and of enzymatic 'remodeling', with as final outcome a scar. In the context of this scheme, the performance of a drug in chronic inflammation would depend on how effectively it inhibited a particular pathway and on the relative importance of the different pathways with respect to tissue destruction and perpetuation of the inflammatory **process**. Presently, there are no quantitative **methods** for weighing the importance of the different components of the inflammatory **process** as outlined above, either in terms of their relative contributions to tissue dysfunction and destruction or in terms of their contribution to the self perpetuating character of chronic inflammation.

L32 ANSWER 31 OF 33 JAPIO COPYRIGHT 2003 JPO
 ACCESSION NUMBER: 2001-329002 JAPIO
 TITLE: MODIFIED **HYALURONIC ACID**
GEL, ITS PREPARING METHOD
AND MEDICAL MATERIAL CONTAINING
SAME
 INVENTOR: HIMEDA KOICHI; UMEDA TOSHIHIKO
 PATENT ASSIGNEE(S): DENKI KAGAKU KOGYO KK
 PATENT INFORMATION:

| PATENT NO | KIND | DATE | ERA | MAIN IPC |
|---------------|------|----------|--------|------------|
| JP 2001329002 | A | 20011127 | Heisei | C08B037-08 |

APPLICATION INFORMATION

STN FORMAT: JP 2000-154943 20000525
 ORIGINAL: JP2000154943 Heisei
 PRIORITY APPLN. INFO.: JP 2000-154943 20000525
 SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined
 Applications, Vol. 2001

AN 2001-329002 JAPIO

AB PROBLEM TO BE SOLVED: To provide a modified **hyaluronic acid gel** which can be obtained by using no crosslinking agent, is excellent in safety and biocompatibility and has controlled solubility, and to provide a **medical material** containing the same.

SOLUTION: A modified **hyaluronic acid gel** is made of only a modified **hyaluronic acid** which is hardly soluble in neutral water.
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L32 ANSWER 32 OF 33 JAPIO COPYRIGHT 2003 JPO
ACCESSION NUMBER: 2000-248002 JAPIO
TITLE: SELF-CROSSLINKED **HYALURONIC ACID**,
ITS **PRODUCTION** AND ITS USE
INVENTOR: ARAI KAZUHIKO; MAEDA KAZUAKI; MIYATA YOSHIAKI
PATENT ASSIGNEE(S): DENKI KAGAKU KOGYO KK
PATENT INFORMATION:

| PATENT NO | KIND | DATE | ERA | MAIN IPC |
|---------------|------|----------|--------|------------|
| JP 2000248002 | A | 20000912 | Heisei | C08B037-08 |

APPLICATION INFORMATION

STN FORMAT: JP 1999-42424 19990219
ORIGINAL: JP11042424 Heisei
PRIORITY APPLN. INFO.: JP 1999-42424 19990219
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 2000

AN 2000-248002 JAPIO

AB PROBLEM TO BE SOLVED: To obtain the subject **hyaluronic acid** having an ideal biological compatibility as a **medicinal material** by partially including a molecular weight fraction having a specific **branched degree**.
SOLUTION: This **hyaluronic acid** is obtained by partially including a molecular weight fraction having ≥ 0.5 **branched degree**. The **hyaluronic acid** in which the **hyaluronic acid** keeps a crosslinked structure and can be distinguished from a linear **hyaluronic acid** in a high polymer solution theory as a **hyaluronic acid** having a branching point. As the molecular weight and the **branched degree**, e.g., among the **method** for using differential refractometer and polyangle laser light scattering detector as a detector in a **gel** permeation chromatogram, by an elution volume **method** calculating a **branched degree** in comparing a molecular weight of **hyaluronic acid** of the same elution volume of fraction to the molecular weight of an objective linear **hyaluronic acid**. The objective **hyaluronic acid** can be formed by, e.g. a **method** for **freezing** an aqueous solution of **hyaluronic acid** having $\text{pH} \leq 3$.
5 and **thawing**.
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L32 ANSWER 33 OF 33 JAPIO COPYRIGHT 2003 JPO
ACCESSION NUMBER: 2000-178304 JAPIO
TITLE: **PRODUCTION OF HYALURONIC ACID GEL**
INVENTOR: OSHIMA KAZUHIRO; OKAMOTO AKIO; MIYATA YOSHIAKI; KAWADA MASATOSHI
PATENT ASSIGNEE(S): DENKI KAGAKU KOGYO KK
PATENT INFORMATION:

| PATENT NO | KIND | DATE | ERA | MAIN IPC |
|-----------|------|------|-----|----------|
|-----------|------|------|-----|----------|

JP 2000178304 A 20000627 Heisei C08B037-08

APPLICATION INFORMATION

STN FORMAT: JP 1998-355527 19981215
ORIGINAL: JP10355527 Heisei
PRIORITY APPLN. INFO.: JP 1998-355527 19981215
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined
 Applications, Vol. 2000

AN 2000-178304 JAPIO

AB PROBLEM TO BE SOLVED: To provide a **hyaluronic acid gel** which can be used as a biocompatible material with a long residence time in the living body, without using any chemical crosslinker or chemical modifier and without forming a composite with a cationic polymer for the best use of the feature, i.e., the excellent biocompatibility inherent in **hyaluronic acid**.
SOLUTION: The **process** for producing a **hyaluronic acid gel** hardly soluble in a neutral aqueous solution comprises **freezing** an acidic **hyaluronic acid** solution made by using a mixture of a polar organic solvent and water as the solvent and having a **pH** of **3.5** or lower, and then **thawing** the solution. The **hyaluronic acid gel** is formed from an acidic **hyaluronic acid** solution of which the concentration of **hyaluronic acid** is at least 5 wt.%, in which the solvent used comprises a mixture of a polar organic solvent and water, and which contains an acid component in an amount at least equimolar to that of the carboxy groups of **hyaluronic acid**.
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FILE 'REGISTRY' ENTERED AT 16:08:46 ON 21 FEB 2003

E HYALURONIC ACID/CN

L18 1 SEA ABB=ON "HYALURONIC ACID"/CN

FILE 'HCAPLUS' ENTERED AT 16:09:10 ON 21 FEB 2003

L19 12762 SEA ABB=ON L18 OR ?HYALURONIC?(W)?ACID?

L20 1653 SEA ABB=ON L19 AND GEL?

L21 857 SEA ABB=ON L20 AND (?PRODN? OR ?PRODUCT? OR ?PREP? OR
?SYNTH?)

L22 342 SEA ABB=ON L21 AND (?METHOD? OR ?PROCED? OR ?PROCES? OR
?TECHNIQ? OR ?TECHNIC? OR ?MECHANISM?)

L23 7 SEA ABB=ON L22 AND (?MEDIC?(W)?MATER?)

L24 25 SEA ABB=ON L22 AND (?FREEZ? OR ?THAW?)

L25 30 SEA ABB=ON L23 OR L24

L26 1 SEA ABB=ON L25 AND PH(L) 3.5
D TI AU

L27 3 SEA ABB=ON L22 AND PH(L) 3.5

L28 32 SEA ABB=ON L25 OR L27

L29 2 SEA ABB=ON L22 AND ?BRANCH?(W)?DEGREE?

L30 32 SEA ABB=ON L28 OR L29

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
16:31:05 ON 21 FEB 2003

L31 39 SEA ABB=ON L30

L32 33 DUP REMOV L31 (6 DUPLICATES REMOVED)

*this yielded some
false drops - sorry!*

*I included these
terms so they would
be highlighted on
the printout*